



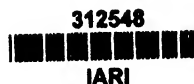
AGRICULTURAL RESEARCH INSTITUTE

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TRANSACTIONS
OF THE
SOCIETY OF TROPICAL MEDICINE
AND HYGIENE.

VOL. VIII.

1914-15.



London:
SOCIETY OF TROPICAL MEDICINE AND HYGIENE,
11, CHANDOS STREET, CAVENDISH SQUARE, W.

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TRANSACTIONS

OF THE

SOCIETY OF TROPICAL MEDICINE

AND HYGIENE.

NOVEMBER, 1914.

VOLUME VIII No. 1.

Proceedings of a Meeting of the Society on Friday, October 21st, 1914.

In the absence of the President, the Chair was taken by
Dr. F. M. SANDWICH, *Vice-President*.

The death of Captain HENRY SHERWOOD RANKEN,, a Fellow of the Society, on the field of battle, was reported to the meeting, and a motion expressing condolence with the members of Captain RANKEN's family was passed. An appreciation of Captain RANKEN's life and work will be found on another page.

CLASSIFICATION OF THE AFRICAN TRYPANOSOMES PATHOGENIC TO MAN AND DOMESTIC ANIMALS.

BY

SURGEON-GENERAL SIR DAVID BRUCE, C.B., A.M.S.

INTRODUCTION.

I have confined myself in this paper to the classification of the more important trypanosomes which affect man and his domestic animals in Africa, chiefly because it is only of these species, or of some of these species, that I have personal knowledge and have studied in the field. It seems to me to be as dangerous to classify trypanosomes from old

laboratory strains, as it would be to attempt to give the natural history of the blue rock pigeon from a study of our tame varieties. Two important species of African trypanosomes, *Trypanosoma evansi* and *Trypanosoma equiperdum*, I have never studied in the field, but nevertheless have placed them in the following scheme of classification from general considerations. One of the most curious results of the study of laboratory strains, has been to classify in separate groups *Trypanosoma brucei* and *Trypanosoma gambiense*, as anyone working with these two species under natural conditions must recognise their close relationship. This is, perhaps, not so strange as it appears, as not only has the laboratory strain of *Trypanosoma brucei* changed its morphology and become monomorphic, but according to ROUBAUD it has also lost its power of undergoing development, or even surviving in the tsetse fly. This is not to be wondered at, as it is now nearly twenty years since this species was first introduced into European laboratories.

In classifying the African pathogenic trypanosomes I have striven for simplicity, as it seems better for practical purposes to divide them into a few defined species rather than to try, with our present incomplete knowledge, to subdivide them more minutely.

The three principal points I have depended upon in this classification of trypanosomes, are morphology, action on animals, and mode of development in the tsetse fly.

At one time I hoped that culture on artificial media might be used as an aid to classification, but up to the present the hope has been unfulfilled. Other methods, such as cross-inoculation experiments and serum diagnosis, I do not consider as much use in making a simple, workable, practical classification, such as will be found of use for diagnosis in the field. If we admit them into our methods, the multiplication of species will proceed to an unmanageable degree.

In the arrangement adopted here it may be asserted that there is no difficulty in distinguishing between the different species by ordinary means in the field, but I defy anyone to differentiate between *Trypanosoma brucei* and *Trypanosoma rhodesiense* or *Trypanosoma gambiense* and *Trypanosoma nigeriense* by any known method, to name only two instances among many from other systems of classification.

In studying and describing trypanosomes it would be well if some standard method were followed by each worker. It is not enough to

say without further description, as I seem to have read somewhere of a trypanosome that was seen in the goat, "as this seems to be a new species the name of *Trypanosoma capræ* is proposed for it." Priority cannot be claimed for a name unless a satisfactory description of the object named has been given. For my part, I have been in the habit for several years of describing the various trypanosomes I have encountered, according to a fixed plan.

A short description of this may be useful to those beginning the study of this branch of protozoology.

I. MORPHOLOGY.

A. Living Unstained.—Under this heading the general appearance and motility of the trypanosome is noted. In regard to motility, care must, of course, be taken to get an average impression from several specimens, since temperature and other factors may interfere.

B. Fixed and Stained.—The blood films are fixed in osmic acid vapour and alcohol, and stained with giemsa. The trypanosomes are drawn at a magnification of 2,000 by means of a camera lucida and then measured.

I see some workers instead of drawing round the circumference of the trypanosome, merely draw a line down the centre. This must save time, but is useless as a record of shape, breadth, etc. Each worker, in fact, has introduced some modification of his own, whereas the crux of the method is uniformity.

Length.—To ascertain the average length of any species of trypanosome, it would be well to draw and measure 1,000 specimens from each susceptible animal, and plot the results into a curve. The thousand specimens should be drawn in sets of one hundred or less on ten or more different days.

The hope that species of trypanosomes could be separated by these curves has not been realised, but still the curve is useful, as it affords a simple means of expressing graphically the length and distribution of length in a given species.

As it is not possible to draw and measure, on an average, more than two hundred trypanosomes in a day, this means, in the case of a trypanosome with ten susceptible animals, an expenditure of fifty days,

or say two months, on this point of length alone. This then, to most workers, is a council of perfection.

A modification of this was introduced by STEPHENS and FANTHAM, who proposed that one animal, the white rat, should be used, and that a hundred trypanosomes should be measured on each of ten consecutive days from their first appearance in the blood, making a thousand in all.

There is a good deal to be said in favour of this as a standard method. The disadvantages are that several important species of trypanosomes do not affect the rat, and that trypanosomes are apt to vary a good deal in their average length by passage through rats. For example, a strain of trypanosomes in Nyasaland was found to vary from 24.2 to 28.6 microns after several passages through white rats. Again, even although each experimental rat was inoculated directly with parasites from the wild game or the tsetse fly, it is possible that no two strains of the same species of trypanosome would shew the same average length or the same curve. The variation from day to day of the average length of the trypanosome in the rat is so great that discordant results constantly occur.

It is evident then that until we know more of the causes of the variations in the length of trypanosomes growing in the blood of experimental animals, that curves shewing the distribution in length will not be of much assistance. *But as length is an important factor in diagnosis, let me suggest that at least one thousand trypanosomes taken at random from various susceptible animals should be drawn and measured by the same standard method, and that when feasible a thousand trypanosomes from a single white rat taken on ten consecutive days from their first appearance in the blood, should also be measured.*

Breadth.—All the trypanosomes drawn should also be measured for breadth. This may be done by measuring across the thickest part of the trypanosome body exclusive of the undulating membrane, but to obtain uniform results it is better to make a rule to measure across the widest part, including the undulating membrane.

Shape.—It is difficult to describe shape in trypanosomes, but, undoubtedly, a well marked difference does exist between them. This is readily seen by examining drawings, when the general impression conveyed by a group of *Trypanosoma brucei* is very different from

that conveyed by a group of *Trypanosoma vivax*. On this account it is always well to include careful coloured drawings in any description of a trypanosome.

Contents of Cell.—The cytoplasm is sometimes clear and hyaline as in the *Trypanosoma vivax* group, or containing granules as in the *Trypanosoma brucei* group.

Nucleus.—May be round or oval, compact or diffused, situated centrally or nearer the posterior or anterior extremities.

Micronucleus.—Large or small, situated terminally or at some distance from the posterior extremity.

Undulating Membrane.—May be well developed and thrown into bold folds, or narrow and simple.

It is probable that the development and disposition of the undulating membrane has much to do with giving the characteristic appearance to different trypanosomes.

Flagellum.—It may project beyond the undulating membrane, when it is called a free flagellum, or terminate at the anterior extremity of the body, when the terms aflagellar or non-flagellar are used. Some species have a free flagellum, others not.

II. THE SUSCEPTIBILITY OF ANIMALS.

This second means at our disposal for the classification or differentiation of trypanosomes has also to be used with prudence.

It is well known that passage through a series of animals of the same species, usually exalts the virulence of the trypanosome towards that animal. For example, *Trypanosoma brucei* after passage through white rats for many generations, kills them in as short a time as two days; whereas the naturally wild strain only kills, on an average, in twenty to thirty days. On the other hand a species, *Trypanosoma simiae*, which in the natural state, as found in the tsetse fly, kills monkeys in ten days, after passage through the goat loses all virulence for the former animals. Another species, *Trypanosoma capræ*, may in a state of nature be incapable of infecting rodents, but by educating them for some time they can at last be made quite virulent for rabbits.

But if a trypanosome is caught in its wild state and put through a series of animals, the result is, in my opinion, of some use in differentiating species. For example, *Trypanosoma brucei* will be found much more virulent than *Trypanosoma gambiense*.

In regard to the number of animals to be inoculated, I think, if possible, a minimum of ten of each species should be used. This, of course, in the case of large animals, such as horses and cattle, is not always possible, as the expense is too great, but this number should be aimed at. It is especially in the case of the larger domestic animals that we wish to know the animal's susceptibility, the rate of mortality, the duration of disease and chances of recovery.

III. THE DEVELOPMENT IN THE INVERTEBRATE HOST.

All the pathogenic trypanosomes of man and his domestic animals, found in Africa, with the exception of *Trypanosoma evansi* and *Trypanosoma equiperdum*, pass through a specific cycle of development in tsetse flies, which are the natural carriers of these diseases. The development in the tsetse fly is different for different species of trypanosomes, and this may be made use of in classification. It is not known whether the North African species, *Trypanosoma equiperdum* and *Trypanosoma evansi*, are capable of developing in tsetse flies. It is possible that on account of disuse they have lost the faculty. It would certainly be an interesting experiment to make.

IV. CROSS-INOCULATION EXPERIMENTS.

This method of differentiating trypanosomes has been much used at the Pasteur Institute by LAVERAN and MESNIL. It is difficult to carry out in the field, as immunised animals are not always procurable, and when carried out with laboratory strains, errors may result on account of the mutability of the virulence of the trypanosomes.

V. SERUM EXPERIMENTS.

These were not found to be very practicable in Central Africa on account of the difficulty, or even impossibility, of keeping up a sufficient supply of the smaller experimental animals, such as tame rats and mice. In fixed stations this might be overcome, but in a temporary camp we always found the keeping up of a sufficient supply of these animals a very practical difficulty.

VI. GEOGRAPHICAL DISTRIBUTION.

This may be useful in some cases, to help in the separation of species of trypanosomes. For my part, I think that the geographical distribution

of Nyasaland sleeping sickness, or *Trypanosoma brucei* disease, is the only way—experiments on man being impracticable—of shewing that *Trypanosoma brucei* and *Trypanosoma rhodesiense* are one and the same species. If in the future, cases of this disease are found in widely separated places where *Glossina morsitans* and wild game abound, then it would be a strong argument that this form of sleeping sickness is caused by *Trypanosoma brucei*. I have left out such species as *Trypanosoma lewisi*, *Trypanosoma theileri*, and *Trypanosoma ingens*, as they are of no practical pathological importance.

With these few preliminary remarks, let me proceed to detail my classification of the pathogenic trypanosomes of Africa.

I have divided them into three groups.

A. Group. Trypanosoma brucei group:—

1. *Trypanosoma brucei*.
2. *Trypanosoma gambiense*.
3. *Trypanosoma evansi*.
4. *Trypanosoma equiperdum*.

B. Group. Trypanosoma pecorum group:—

1. *Trypanosoma pecorum*.
2. *Trypanosoma simie*.

C. Group. Trypanosoma vivax group:—

1. *Trypanosoma vivax*.
2. *Trypanosoma capræ*.
3. *Trypanosoma uniforme*.

These constitute all the principal, important trypanosomes discovered up to the present time in Africa.

With the exception of *Trypanosoma evansi* and *Trypanosoma equiperdum*, they are all carried from sick to healthy animals by means of tsetse flies. I have placed these two species in the first group as they seem by morphology and their action on animals to belong there.

Each group is distinguishable or separable by well defined characters.

Group A. The Trypanosoma brucei group.—The species of trypanosomes forming this group are all more or less polymorphic, varying in shape and size from the short and stumpy, non-flagellar forms, to long and slender forms with free flagella. The cytoplasm contains numerous

dark staining granules. The micronucleus is small and is situated as a rule some distance from the posterior extremity. The undulating membrane is well developed and thrown into bold folds.

Two of the members of the group develop in the tsetse flies in the same way, but whether the other two can or cannot is unknown. At first the development takes place in the intestine, afterwards the parasites pass into the salivary glands, and there complete their development into infective forms.

This group can be separated from the other groups by shape alone.

Group B. The Trypanosoma pecorum group.—The trypanosomes are small and monomorphic. The cytoplasm is non-granular. The micronucleus is prominent, sub-terminal, and often seems to project beyond the margin. The undulating membrane is fairly well developed.

The cycle of development takes place in the intestinal tract and the proboscis—the labial cavity and hypopharynx—of the fly, but does not reach the salivary glands.

Group C. The Trypanosoma vivax group.—The trypanosomes are monomorphic and very active in their movements. The posterior extremity is enlarged. The cytoplasm is clear and hyaline. The micronucleus is large and terminal. The undulating membrane is little developed and simple. The development in the invertebrate host takes place in the labial cavity and hypopharynx of the proboscis of the fly, but not in the intestinal tract or salivary glands.

These three groups are well marked, and it is fairly easy to separate them in the blood of the vertebrate host, or even in the invertebrate host, by microscopic examination alone.

Group A.

1. *TRYPANOSOMA BRUCEI* (PLIMMER AND BRADFORD, 1899)

Synonyms: Trypanosoma rhodesiense. (Stephens and Fantham, 1910.)

Trypanosoma ugandæ. (Stephens and Blacklock, 1913.)

I. MORPHOLOGY.

Length and Breadth.—*Trypanosoma brucei* varies from 12 to 35 microns—average 21—in length, and from 1·5 to 5·5—average 3·18—in breadth.

Shape.—This species is markedly dimorphic, some forms being short and stumpy, while others are long and slender. The posterior extremity of the short forms is often blunt, broad and square, or even emarginate.

Contents of Cell.—The protoplasm is usually dotted over with numerous chromatin granules, especially in the anterior half.

Nucleus.—Is oval or elongated in the long and slender forms, and round or oval in the short and stumpy forms. *In the short forms it is frequently found situated far back near the micronucleus, or even posterior to it. These varieties are known as posterior nuclear forms, and serve to distinguish Trypanosoma brucei from Trypanosoma gambiense and Trypanosoma evansi. Trypanosoma equiperdum resembles Trypanosoma brucei in this character.*

Micronucleus.—Small and round, situated, on an average, 2·1 microns from the posterior extremity in the long and slender forms, and 1·1 in the short and stumpy forms.

Undulating Membrane.—This is well developed, and thrown into bold folds or undulations.

Flagellum.—The flagellum in the long and slender forms is free, and, on an average, 6 microns in length. In the short and stumpy forms there is no free flagellum.

II. ANIMALS SUSCEPTIBLE TO *TRYPANOSOMA BRUCEI*.

Animals of many different species are attacked by *Trypanosoma brucei*. The disease it gives rise to is acute in some, and chronic in others.

The following table gives the duration of the disease in various animals. It is unfortunate that the strain used is not taken direct from wild game or tsetse fly, but is one which had been preserved for some time in the Pretoria laboratory, Transvaal, by passage through horses and cattle. It came originally from Zululand, and was first studied by Mr. SHILSTON, at Pietermaritzburg, in Natal.* Duration of disease includes incubation. R. stands for refractory.

* Description of a strain of *Trypanosoma brucei* from Zululand. Pro. Royal Society B. vol. 87, p. 493.

	Duration of disease in days.	No. of animals used.	Remarks.
Man	90	?	Nyasaland Sleeping Sickness.
Horse	38	3	No recoveries.
Ox	134	1	Chronic, may recover.
Goat and sheep	42	29	Chronic, may recover.
Baboon	R.	1	Not susceptible.
Monkey	26	20	Acute.
Dog	34	25	Acute.
Rabbit	28	7	Acute.
Guinea-pig	67	15	Chronic.
White Rat	30	21	Acute.

This species is much more rapidly fatal than *Trypanosoma gambiense*, and this forms one of the main characters by which the two species can be separated.

III. THE DEVELOPMENT OF TRYPANOSOMA BRUCEI IN THE TSETSE FLY.

The carrier of *Trypanosoma brucei* in Africa is the common tsetse fly, *Glossina morsitans*. The development takes place first in the intestinal tract of the fly. After some twenty or thirty days the trypanosomes pass forward through the labial cavity and from there by way of the hypopharynx into the salivary glands, where they multiply to an extraordinary extent.

The trypanosomes undergoing development in the intestinal tract are not capable of giving rise to the disease. It is only when they reach the salivary glands that they assume the original blood form and become infective.

STEPHENS and FANTHAM in making *Trypanosoma rhodesiense* a new species, depended altogether on the presence of posterior nuclear forms to separate it from the other members of this group. Now that it is known that *Trypanosoma brucei* and *equiperdum* have just as many of these posterior nuclear forms, it would seem to be their duty either

to withdraw this species or to give some other mark by which it may be recognised. I have already brought up arguments in favour of my contention that *Trypanosoma brucei* and *Trypanosoma rhodesiense* are one and the same,* so that it seems unnecessary to recapitulate them here.

In regard to *Trypanosoma pecaui* there is evidently a good deal of confusion as to what is meant. It is usually described as a dimorphic species similar to *Trypanosoma brucei*. ROUBAUD, however, states that it develops in the intestine and proboscis, but does not reach the salivary glands. If this is so, then *Trypanosoma pecaui* cannot belong to the *Trypanosoma brucei* group but to the *Trypanosoma pecorum* group.

2. *TRYPANOSOMA GAMBIENSE* (DUTTON, 1902).

Synonym: Trypanosoma nigeriense. (Macfie, 1913.)

1. MORPHOLOGY.

This species resembles *Trypanosoma brucei* very closely. There are the same long and slender, intermediate, and short and stumpy forms in both.

Length and Breadth.—*Trypanosoma gambiense* varies in length from 13 to 37 microns. The average of a thousand, taken at random, was 22.1. The breadth varies from 1.25 to 4.75. Average, 2.81.

Shape.—*Trypanosoma gambiense* resembles *Trypanosoma brucei* in most respects, but there is an absence among the short and stumpy of the posterior nucleated, coarse, heavy forms, which are such a feature in the latter. At present it is believed that *Trypanosoma brucei* can be differentiated from *Trypanosoma gambiense* and *Trypanosoma evansi*, by this characteristic, but this would certainly require the study of many blood films from various animals and could not be done, for example, by the microscopic examination of a single slide. It would certainly be useful if the direct examination of the trypanosomes, in the blood of a case of sleeping sickness, should let us know whether we are dealing with a case of Congo or Nyasaland sleeping sickness. At present I am afraid this is not possible.

* Departmental Committee on Sleeping Sickness, presented to Parliament. June, 1914. (Cd. 7350). Wyman & Sons, p. 238.

Contents of Cell.—The cytoplasm contains many dark stained granules especially in the anterior half.

Nucleus. *Posterior nucleated forms are rare or absent.*

Micronucleus, Undulating membrane and Flagellum are similar in all the members of this group.

II. ANIMALS SUSCEPTIBLE TO TRYPANOSOMA GAMBIENSE.

Trypanosoma gambiense attacks several species of animals, but is less virulent than Trypanosoma brucei or Trypanosoma evansi. Both in Uganda and Nyasaland we found great difficulty in starting an infection in the lower animals. It often required repeated injections before a successful result could be obtained. The duration of the disease in experimental animals is also much longer than in the case of *Trypanosoma brucei*. This, in my opinion, is one of the most useful characters in the differentiation of the two species.

The following table gives a list of various animals with the duration of the disease :—

	Duration of disease in days.	No. of animals used.	Remarks.
Man	2 to 5 yrs.	—	May be less than two years.
Oxen	R.	--	May act as reservoir.
Goats	R.	18	May act as reservoir
Antelope	R.	---	May act as reservoir.
Monkeys	200	19	Eight never shewed trypanosomes.
Dogs	100	13	Nine never shewed trypanosomes.
Guinea-pigs	264	13	One only shewed trypanosomes.
Rats	135	25	Ten never showed trypanosomes.

III. THE DEVELOPMENT OF TRYPANOSOMA GAMBIENSE IN THE TSETSE FLY.

The development of *Trypanosoma gambiense* in *Glossina palpalis* is similar to that of *Trypanosoma brucei* in *Glossina morsitans*.

3. *TRYPANOSOMA EVANSI* (STEEL 1885).*Synonym: Trypanosoma soudanense (Laveran, 1907.)*

I. MORPHOLOGY.

As I have never studied this species in the field, I can only give a description of it from laboratory strains. No full description of this species, as far as I can remember, has been made from specimens taken under natural conditions.

Length.—Varies between 18 and 34 microns. Average, 24·9.

Shape.—*Trypanosoma evansi* resembles *Trypanosoma brucei* and *Trypanosoma gambiense* in general appearance. In the laboratory strain described by me in 1911,* there were very few short and stumpy individuals found, but there were some, and this justifies the inclusion of this species in the dimorphic group. To put *Trypanosoma evansi* in a group separate from *Trypanosoma brucei* and *Trypanosoma gambiense* would be a most unnatural grouping, as the most cursory examination of these three species discloses the close relationship which exists between them. It is probable if strains of *Trypanosoma evansi* were studied in the field the percentage of short and stumpy forms would be found increased. In the laboratory strain there was a total absence of the posterior-nucleated blunt-ended forms found in *Trypanosoma brucei*.

Contents of Cell.—According to LAVERAN and MESNIL and others, a large proportion of *Trypanosoma evansi* shew no distinct granules in front of the nucleus, whereas the majority of *Trypanosoma brucei* do. Moreover, when granules are present in the former, they are, as a rule, neither so large, nor so numerous, nor so deeply stained, as in the latter.

In regard to the *nucleus*, *micronucleus*, *undulating membrane*, and *flagellum*, I am not aware that these parts differ in any way from the other members of the group,

II. ANIMALS SUSCEPTIBLE TO *TRYPANOSOMA EVANSI*.

Trypanosoma evansi principally attacks elephants, horses, donkeys, camels, and dogs. It seems to be an extremely chronic disease in cattle, goats, and sheep. The smaller experimental animals succumb readily.

* Proceedings of Royal Society, B. vol. 83.

	Duration of disease in days.	Mortality.	Remarks.
Horse	52	100%	Steel. From 6 to 54 (Lingard).
Mule	19	—	Steel.
Elephant ..	"	?	Not recorded.
Camel	1000	?	
Cattle	?	20%	Chronic. Mauritius.
Goats	150	—	Usually recover (Laveran & Mesnil).
Sheep	150	—	Usually recover (Laveran & Mesnil).
Dogs	30	—	Lingard.
Rabbit	35	—	Edington.
Guinea-pig	34	100%	Laveran and Mesnil.
Rats	11	100%	Laveran and Mesnil.
Pigs	R.	R.	

III. DEVELOPMENT OF *TRYPANOSOMA EVANSI* IN THE INVERTEBRATE HOST.

No cycle of development has been discovered in any invertebrate host.

4. *TRYPANOSOMA EQUIPERDUM* (DOFLEIN, 1901).

A trypanosome disease of horses in North Africa, Europe, India, and North America.

I. MORPHOLOGY.

This species evidently belongs to the *Trypanosoma brucei* group, as it is dimorphic, and among the short and stumpy forms YORKE and BLACKLOCK report that a considerable percentage of posterior nucleated examples are present.

Length. According to the same authors *Trypanosoma equiperdum* varies in length from 15 to 36 microns. Average, 26·7.

Breadth. Not recorded.

The presence of posterior nucleated forms would seem to separate this species from *Trypanosoma gambiense* and *Trypanosoma evansi*, but I am not aware of any morphological features which would differentiate it from *Trypanosoma brucei*.

II. ANIMALS SUSCEPTIBLE TO *TRYPANOSOMA EQUIPERDUM*.

Trypanosoma equiperdum only attacks horses and donkeys, and of these

only the stallions and mares, geldings are never attacked. It is always difficult to locate or find in the horse, and never occurs in the general circulation. Other animals may be infected by artificial inoculation. This disease is so different from that caused by *Trypanosoma brucei*, that there can be no difficulty in diagnosis.

Group B.

1. TRYPANOSOMA PECORUM.

Synonyms: Trypanosoma confusum. (Kingham and Montgomery.)

Trypanosoma nanum. (Laveran.)

It is probable that *Trypanosoma dimorphon* (LAVERAN and MESNIL), and *Trypanosoma congolense* (BRODEN), of the East Coast, are closely allied to this species: they certainly belong to this group.

I. MORPHOLOGY.

This is the smallest of all the African pathogenic trypanosomes. It is probably the most important trypanosome disease, in Africa, among bovines.

Length and Breadth.—*Trypanosoma pecorum* varies from 9 to 18 microns in length. Average, 14. In breadth it averages 1.96.

Shape.—This species is monomorphic, and short and stout in form.

Contents of Cell.—Generally homogeneous.

Nucleus.—Oval in shape, and situated about the middle of the body.

Micronucleus.—Small and round, and situated near to but not at the posterior extremity, and often projecting beyond the edge of the trypanosome.

Undulating Membrane.—Simple, but fairly well developed.

Flagellum.—There is no free flagellum.

II. ANIMALS SUSCEPTIBLE TO TRYPANOSOMA PECORUM.

Horses, donkeys, oxen, goats, sheep, pigs, dogs, guinea-pigs, rats, etc., are susceptible to this disease.

Trypanosoma pecorum readily loses its virulence for certain animals by passage through certain other animals. For example, if this species—which is usually more or less infective to the monkey, dog, and rat—lives for some time in the blood of the goat, it loses its power of infecting the former animals. This has given rise to the erroneous idea that a separate species, *Trypanosoma nanum*, exists. *Trypanosoma*

nanum is, in truth, nothing but a strain of *Trypanosoma pecorum*, which has lost its virulence for the other animals, by its passage through the goat or allied animal.

The following table gives the average duration of this disease in various species of animals :—

	Average duration in days.	No. of animals used.	Remarks.
Donkeys .. .	87	1	Many recover.
Cattle...	121	4	
Goats	55	59	A few recover.
Pigs .. .	21	1	
Monkeys .. .	129	11	None recover.
Dogs	48	57	None recover.
Guinea-pigs...	41	5	None recover.
Rats	33	10	None recover.

III. THE DEVELOPMENT OF TRYPANOSOMA PECORUM IN THE INVERTEBRATE HOST.

The chief carrier of *Trypanosoma pecorum* is *Glossina morsitans*. The development takes place first in the gut, then the trypanosomes pass forward into the labial cavity of the proboscis and finally reach the hypopharynx, where the trypanosomes revert to the original blood forms and become infective. There is no infection of the salivary glands.

2. TRYPANOSOMA SIMIÆ.

Synonym : *Trypanosoma ignotum*. (Kinghorn and Yorke).

I. MORPHOLOGY.

Trypanosoma simiæ is like *Trypanosoma pecorum* in general appearance, and in fact it is often difficult or impossible to distinguish between a short individual of the former species and a long one of the latter.

Length.—*Trypanosoma simiæ* varies in length from 14 to 24 microns. Average, 17·5.

As in *Trypanosoma pecorum* there is the same well developed undulated membrane, the same oval nucleus situated about the middle of

the body, and the same excentrically placed micronucleus often appearing to project beyond the margin.

II. ANIMALS SUSCEPTIBLE TO *TRYPANOSOMA SIMIÆ*.

An interesting feature in this trypanosome is the virulence it displays towards monkeys and the domestic pig, killing these animals in an incredibly short period of time, whereas it is harmless to oxen, antelope, dogs, and the smaller experimental animals such as the rabbit, guinea-pig and rat. Curiously enough this trypanosome also infects goats and sheep, although cattle and antelope escape.

Another interesting point about this species is that, as far as is known, the wart-hog is the only animal among the wild game which harbours it.

The rapidity with which the virulence of *Trypanosoma simiæ* becomes modified is also remarkable. When a cage of *wild Glossina morsitans* is placed on a monkey and a goat, both animals take the disease, and the monkey in such an acute form that the average duration of life is only a few days. But if it is attempted to pass *Trypanosoma simiæ* from an infected goat to a healthy monkey, by inoculation of the goat's blood, the experiment usually fails, shewing that a short sojourn in the blood of the goat has almost nullified the virulence of the parasite for the monkey.

The following table gives the average duration of life in various animals. R. means refractory :—

	Average duration of days.	No. of animals used.	Remarks.
Cattle... ..	R.	4	
Antelope	R.	5	
Goats and Sheep ...	46·6	5	About half recover.
Pigs	5·3	9	None recover.
Baboon	R.	3	
Monkeys	10·8	24	Rapidly fatal.
Dogs	R.	21	
Rabbits	R.	10	
Guinea-pigs	R.	5	
Rats	R.	8	

III. THE DEVELOPMENT OF *TRYPANOSOMA SIMIÆ* IN THE INVERTEBRATE HOST.

The carrier of *Trypanosoma simiæ* is *Glossina morsitans*. The development in the fly is identical with *Trypanosoma pecorum*, first in the gut and then in the labial cavity and hypopharynx of the fly. There is no infection of the salivary glands.

Group C.

1. *TRYPANOSOMA VIVAX* (ZIEMANN, 1905).

Synonym: Trypanosoma cazalbouri (Laveran, 1906).

I. MORPHOLOGY.

A. Living Unstained.—This species of trypanosome is extremely active in its movements. It dashes across the field of the microscope with such rapidity that it is impossible to follow its movements. If it remains at one spot for a time, as it sometimes does, it has an appearance of great energy and power, throwing the surrounding red blood corpuscles about.

B. Fixed and Stained.—*Length.*—*Trypanosoma vivax* varies from 16 to 29 microns in length. Average, 24·1.

Shape.—This species can be recognised with certainty by its shape alone. The body of the creature lies mostly posterior to the nucleus, and this part of the body is broad and swollen and filled with beautifully clear protoplasm, in which a delicate alveolar structure can be made out. The body narrows at the nucleus and tapers off rapidly to the anterior extremity.

Contents of Cell.—Clear, with a delicate alveolar structure, and now and then a chromatin-staining granule, especially in the narrow anterior part.

Nucleus.—Often has a diffuse or broken up appearance, situated towards the anterior extremity.

Micronucleus. Large, round and terminal.

Undulating Membrane. Narrow, simple, straight, and little in evidence.

Flagellum. There is a well marked flagellum, the free part varying from 3 to 6 microns in length.

II. ANIMALS SUSCEPTIBLE TO *TRYPANOSOMA VIVAX*.

Equines and ruminants are affected by this species. Monkeys, dogs, and the smaller experimental animals escape.

The following table shews the average duration of life in various animals. R. stands for refractory :—

	Average duration in days.	No. of animals used.	Remarks.
Cattle... ..	89	17	Seldom recover.
Goats... ..	56	12	Seldom recover.
Monkeys	7	R.	
Dogs	5	R.	
Guinea-pigs... ..	4	R.	
Rats	4	R.	
Mice	4	R.	

III. DEVELOPMENT OF *TRYPANOSOMA VIVAX* IN THE INVERTEBRATE HOST.

The carrier of *Trypanosoma vivax* is *Glossina palpalis*. The cycle of development has its seat in the labial cavity of the proboscis. Later the trypanosomes pass into the hypopharynx where they complete their development, reverting to the blood forms and becoming infective. No development takes place in the intestines or salivary glands.

2. *TRYPANOSOMA CAPRÆ* (KLEINE).

I. MORPHOLOGY.

A. Living Unstained.—The description given of *Trypanosoma vivax* can be equally applied to this species. It is just as active in its movements and dashes across the field of the microscope with the same impetuosity.

B. Fixed and Stained.—*Length.*—*Trypanosoma capræ* varies in length from 18 to 32 microns. Average, 25·5.

Breadth.—Measured across the broadest part, *Trypanosoma capræ* varies from 1·75 to 4·35 microns. Average, 3.

Shape.—*Trypanosoma capræ* differs from *Trypanosoma vivax*, in that it is heavier built and altogether has a larger and clumsier appearance. The posterior half is swollen and its end is bluntly angular or rounded. The anterior part is narrower and pointed.

Contents of Cell.—Clear, with a delicate alveolar structure, and free from vacuoles and granules.

Nucleus.—Oval, compact, and lying about the middle of the body.

Micronucleus.—Large and round, situated, as a rule, close to the posterior extremity, but sometimes removed to a short distance.

Undulating Membrane.—More developed than in *Trypanosoma vivax*, and thrown into bolder folds or undulations.

Flagellum.—There is a well marked free flagellum which varies in length from 4 to 9·5 microns. Average, 6·5.

II. ANIMALS SUSCEPTIBLE TO TRYPANOSOMA CAPRÆ.

The following table gives the average duration of life in various animals. R. stands for refractory.

	Average duration in days.	No. of animals used.	Remarks.
Cattle... ..	?	2	Both recovered.
Goats... ..	?	36	Some recover.
Sheep... ..	115·3	4	Some recover.
Monkeys... ..	R.	12	Not susceptible.
Dogs... ..	R.	12	Not susceptible.
Guinea-pigs..	R.	2	Not susceptible.
Rats	R.	2	Not susceptible.

III. THE DEVELOPMENT OF TRYPANOSOMA CAPRÆ IN THE INVERTEBRATE HOST.

The development resembles that of *Trypanosoma vivax*, and takes

place in the labial cavity and hypopharynx of *Glossina morsitans*, and not in the intestines or salivary glands.

3. TRYPANOSOMA UNIFORME.

I. MORPHOLOGY.

A. Living Unstained.—This a small and active trypanosome, which has a marked translatory movement in the field of the microscope. This movement, however, is not to be compared with that of *Trypanosoma vivax* in point of rapidity or range.

B. Fixed and Stained.—*Length.*—*Trypanosoma uniforme* varies in length from 12 to 19 microns. Average, 16.

Breadth.—1·5 to 2·5 microns.

Shape.—This species of trypanosome seems to differ in shape from *Trypanosoma vivax* in that there is not the marked narrowing of the anterior extremity. The posterior extremity is rounded or blunt. These trypanosomes are markedly uniform in appearance, hence the name.

Contents of Cell.—Resembles *Trypanosoma vivax* in shewing a clear protoplasm with fine alveolar structure.

Nucleus.—Oval in shape and compact, not diffuse. It is also seen to be placed about the centre of the body, and does not take up the whole width of the cell as in *Trypanosoma vivax*.

Micronucleus.—Resembles the other members of the group in being large, round and terminal.

Undulating Membrane.—Narrow and little developed.

Flagellum.—There is a well-marked free flagellum, the free part varying from 2 to 5 microns in length.

II. ANIMALS SUSCEPTIBLE TO TRYPANOSOMA UNIFORME.

This species, like the other two, only affects cattle, goats and sheep. It is probably also pathogenic to horses, mules and donkeys, but there is no record of this.

The following table gives the average duration of life in various animals. R. stands for refractory.

	Average duration of days.	No. of animals used.	Remarks.
Cattle... ..	56	4	Two died.
Goats... ..	29	4	Three died.
Sheep... ..	46	3	One died.
Monkey	R.	1	Not susceptible.
Dog	R.	1	Not susceptible.
Guinea-pig	R.	1	Not susceptible.
Rat	R.	1	Not susceptible.
Mouse	R.	1	Not susceptible.

III. THE DEVELOPMENT OF TRYPANOSOMA UNIFORME IN THE VERTEBRATE HOST.

This, as in the other members of the group, is restricted to the proboscis.

DISCUSSION.

Professor J. W. W. STEPHENS: (1) I should like to warn readers of this paper against accepting as truth statements made in a dogmatic form. The following example will shew the necessity for this:—

BRUCE (Col. Sir D.) and others.—“The Development of *Trypanosoma gambiense* in *Glossina palpalis*.” Proceedings of the Royal Society. B. July 5, 1909. Vol. 81, p. 406.

“The mechanical transference of the disease is proved up to the hilt, and for every case which falls a victim to the rare late-infected fly, a thousand must be infected by direct mechanical transference.”

BRUCE (Col. Sir D.), HAMERTON (A. E.), BATEMAN (H. R.) and MACKIE (F. P.).—“Mechanical Transmission of Sleeping Sickness by the Tsetse-fly.” Proceedings of the Royal Society. B. June 30, 1910. Vol. 82, p. 401.

“Mechanical transmission plays a much smaller part, if any, in the spread of sleeping sickness than has been supposed.”

(2) The paper appears to me to suffer from a lack of recognition of the work of other observers. Anyone who wishes to consider impartially

the question of the classification of trypanosomes should study such work. I give here a brief summary of such work which I contributed to the Report of the Departmental Committee on Sleeping Sickness, 1914 :—

I. MORPHOLOGICAL.

If we accept morphological identity as constituting specific identity, then the following trypanosomes, viz.: 1, *T. pecaui*, LAVERAN, 1907; 2, *T. equi*, BLACKLOCK and YORKE, 1913, syn., *T. equiperdum* (*pro parte*); 3, *T. ugandæ*, STEPHENS and BLACKLOCK, syn., *T. brucei*, Uganda; 4, *T. rhodesiense*, STEPHENS and FANTHAM, 1910, syn., *T. brucei* vel *rhodesiense*, are identical, but certain objections to this view may be mentioned :—

1. The trypanosome of the rat (*T. lewisi*) and the trypanosome of the hamster (*T. rabinowitschi*) are stated to be morphologically identical, but it is generally admitted that they are specifically distinct.

2. If dourine is really produced by the dimorphic trypanosome, *T. equi*, then, as *T. rhodesiense* is morphologically identical with it, they are one and the same trypanosome, which is a *reductio ad absurdum*.

3. If all these trypanosomes with posterior nuclei morphologically identical are specifically identical, then it is difficult to understand—

(a) Why, so far as is known, sleeping sickness of the *rhodesiense* type does not occur in West Africa, where dimorphic trypanosomes with posterior nuclei occur.

(b) Why, so far as is known, it does not occur in the French Sudan, where dimorphic trypanosomes with posterior nuclei (*T. pecaui*) occur.

(c) Why, so far as is known, it does not occur in Zululand, where morphologically identical trypanosomes occur.

II. BIOLOGICAL.

These are open to criticism, and are by no means universally accepted, but, I consider, cannot be entirely set aside, for in no case have the biological tests asserted *identity* where the trypanosomes are distinguishable, e.g. :—

	Morphologically.		Biologically.		Authority.
<i>T. rhodesiense</i> and ...	Distinct ...		Distinct ...		MESNIL and
<i>T. gambiense</i>					RINGENBACH.
<i>T. brucei</i> , Zululand, ...	Distinct ...		Distinct ...		MESNIL.
and <i>brucei</i> , Uganda					

On the other hand, there is discrepancy between the morphological and biological tests in the case of trypanosomes morphologically *indistinguishable*, e.g. :—

		Morphologically.		Biologically.		Authority.
<i>T. lewisi</i> and	...	Indistinguishable	...	Distinct	...	Various.
<i>T. rabinowitschi</i>						
<i>T. brucei</i> , Zululand, ...		Indistinguishable	...	Distinct	...	LAVERAN.
and <i>T. evansi</i> (STEELE)						
<i>T. pecaudi</i> and	...	Indistinguishable	...	Distinct	...	MESNIL
<i>T. ugandæ</i>						and LEGER.
<i>T. rhodesiense</i> and	...	Indistinguishable	...	Distinct	...	BECK.
trypanosome of mule,						
Rovuna, G.E. Africa						
<i>T. rhodesiense</i>	...	Indistinguishable	...	Development..		ROUBAUD
				in gut and sali-		and
and				vary <i>glands</i> of		BOUET.
				tsetse-fly		
<i>T. pecaudi</i>	...	Indistinguishable	...	Development		
				in gut and		
				<i>proboscis</i>		

(3) Let “those beginning the study of this branch of protozoology” begin by considering *very carefully* what exactly is meant by the term “*Trypanosoma brucei*.”

Dr. H. B. FANTHAM: I have been much interested in reading a proof of Sir DAVID BRUCE's paper, and I have much pleasure in thanking him for his contribution to a difficult subject, so difficult in fact that in our present incomplete state of knowledge it may even be questioned whether the time is ripe for the classification of trypanosomes. As a zoologist I should like to point out that exception must be taken to the terms “aflagellar,” or “non-flagellar” being used when a trypanosome has no free flagellum. Although there is no free portion, yet a flagellum is still present as a border to the undulating membrane. The term “non-flagellar” applies to a Leishmaniform parasite, such as may be found in the internal organs of the host.

As regards retaining *Trypanosoma rhodesiense* as a separate species,

I still think that this should be done until further work has proved the identity or otherwise of *T. brucei* and *T. rhodesiense*. The latter trypanosome can still be described as a human parasite possessing posterior nuclear forms and producing sleeping sickness in man. It must be remembered that certain investigators, among whom are TODD and BRUMPT, state that they have inoculated themselves with *T. brucei* without untoward result.

LAVERAN (1912) immunised a ram and a sheep against different strains of *T. brucei*; when inoculated with *T. rhodesiense* they both acquired acute infections and died. These experiments go to shew that *T. rhodesiense* is not the same as *T. brucei*. Further, Sir DAVID BRUCE himself is far from dogmatic on the identity of *T. brucei* and *T. rhodesiense* in his evidence before the recent Departmental Committee on Sleeping Sickness.

As regards *T. pecaudi*, I have worked personally with this organism in Khartoum. It is certainly dimorphic and would seem to be removed, by this character alone, from a clearly monomorphic trypanosome like *T. pecorum*. Incidentally, it may be noted that *T. pecorum* is probably the same as *T. congolense* (BRODEN, 1914), and that the latter name should have priority.

Regarding the statement that "the laboratory strain of *T. brucei* has changed its morphology and become monomorphic," I believe that researches on this very important subject have been published recently by BRAUN and TEICHMANN (1914), and by OEHLER (1914). I should like to ask Sir DAVID BRUCE if he knows of any other papers bearing on this most important question, so important in fact that if it be shewn to be of wide application, then it would seem quite unnecessary to maintain laboratory strains of trypanosomes at so much care and expense. Indeed, it would then be imperative to examine each species of trypanosome direct from Nature, and we should be drawn very much nearer to the ideal of a universal trypanosome, possibly like *T. lewisi* or *T. rotatorium*, which has already been suggested by ALEXEIEFF.

In the paper an interesting and unexpected statement concerning the nucleus of *T. gambiense* appears, namely, that "posterior nucleated forms are rare or absent." May I ask if the author has seen *any* posterior nuclear forms in *T. gambiense*?

Again, it is stated that "no cycle of development of *T. evansi* has

been discovered in any invertebrate host." This is hardly so, for it is known that certain species of *Tabanus* and *Stomoxys* transmit *T. evansi*, and some of the Indian investigators, (e.g. BALDREY, 1911) have recorded and figured developmental stages of the trypanosomes in these flies.

Regarding the much discussed curves of lengths of trypanosomes, there can be no doubt that, if such curves are used, they should be made from trypanosomes inoculated into a standard animal, such as a white rat, and that the parasites should be taken and measured on consecutive days from their first appearance in the blood, for the polymorphism of trypanosomes like *T. rhodesiense* and *T. gambiense* is due to the phenomena of growth and division.

MISS ROBERTSON: I was much interested in Sir DAVID BRUCE's paper, and should like to mention one or two points. He mentions that measurement is very valuable in the question of diagnosis. Measurement is very valuable if only in one point, namely, the fixing of the minimum and maximum length of the trypanosome. In some cases this is very helpful in making the diagnosis.

SIR DAVID BRUCE says that 1,000 trypanosomes should be measured. If a smaller number (300 to 500) are measured upon different days, I think it is sufficient. It is very important that the samples should be taken from blood drawn upon different days.

The most important part of this paper is the general soundness of the division into groups. Sir DAVID BRUCE did not emphasise enough that this division is so clearly borne out in the development of the organisms in the invertebrate host. Questions may be raised on specific points, but the general soundness of these three groups is clear, the distinction depending not only upon the morphology in the vertebrate host, but also upon the position in the fly of what has been called the "anterior station," i.e., where the final development occurs. Thus, in Sir DAVID BRUCE's Group A, development is first in the gut and finally in the salivary glands; in Group B, first in the gut and finally in the proboscis; and in Group C the whole development is in the proboscis alone.

The posterior nuclear question has been raised, and while it can be used as a generally convenient landmark when dealing with *T. brucei* and *T. gambiense*, it is doubtful if one can look upon such a character as

of true specific value. It has been suggested by some of the results that this displacement of the nucleus is a physiological reaction to environmental conditions, and may be connected with the rate of division of the trypanosomes. I think that this particular part of the subject might be spoken of by Dr. WENYON, as some of his work has dealt with this question.

A very important point is raised in regard to *T. evansi*. It is very difficult to get sound evidence as to whether the *T. brucei* brought to this country in 1896 and the *T. brucei* we now find representing this strain are really identical. If, however, there has been no error, and a definite change in type has occurred, it is of the utmost importance. I note with great interest that Sir DAVID BRUCE said that he occasionally found short forms in his 1911 strain of *T. evansi*. I remember an account of a similar case occurring in work from Khartoum. I think it was in a paper by Captain FRY in the Wellcome Research Reports. He states that he found rare short forms derived from camels suffering from *T. evansi*. In both cases the diagnosis of the trypanosome as *T. evansi* was apparently made upon sufficient grounds. It is very interesting to find these occasional short forms turning up in *T. evansi*, and it suggests that *T. evansi* may be similar to the laboratory strain of the 1896 *T. brucei*.

I should like to ask Sir DAVID BRUCE about this experiment with *T. simiae*, where he took wild *G. morsitans* and put them into a monkey and a goat—the monkey took the disease in an acute form, whereas the goat shewed only a mild infection. Is the morphology of *T. simiae* and *T. pecorum* sufficiently distinctive to be quite sure that the monkey was not infected with *T. simiae* and the goat with *T. pecorum*?

Professor W. YORKE: I have perused this paper with considerable interest, all the more so since about a year ago I, in conjunction with Dr. BLACKLOCK, attempted to do something similar myself; I think, therefore, I can claim to have given considerable care and attention to the subject.

I was particularly impressed with the following sentence: "Priority cannot be claimed for a name unless a satisfactory description of the object named has been given." At first sight that seems excellent, but when we come to consider the point it seems to me the whole

subject turns upon this question, What can be considered a satisfactory description? What is perfectly satisfactory now may not be regarded as satisfactory in ten years' time, and, conversely, what was considered satisfactory ten years ago may not necessarily be considered so to-day. Arising out of that point, I should like to refer for a moment to the subject of *T. brucei*. I should like to ask Sir DAVID BRUCE if he considers that the existence of individuals without a free flagellum, and other individuals exhibiting typical posterior nuclei may be regarded as characteristic of *T. brucei*. If Sir DAVID BRUCE says he does not consider these characteristics of *T. brucei*, I ask him how he proposes to distinguish between *brucei* and *evansi*, which was described by STEELE in 1885. If Sir DAVID BRUCE tells us he does consider this point essential, I say to him it is obvious the description given by PLIMMER and BRADFORD to *T. brucei* is not satisfactory. PLIMMER and BRADFORD mention nothing about free flagella forms, nor do they refer to posterior nuclear forms, hence, according to Sir DAVID BRUCE's own postulate, priority cannot be given to the name *T. brucei*, but it should go to *T. rhodesiense*, in which these characteristics were clearly brought out by STEPHENS and FANTHAM in 1910. Now Sir DAVID BRUCE says he holds it to be the duty of STEPHENS and FANTHAM to withdraw this species, or give some other mark by which it may be recognised. I rejoin that it is not the duty of them to withdraw the name, but that it is the duty of Sir DAVID BRUCE to advise the withdrawal of the term *T. brucei*, because this trypanosome should be called *T. evansi* or *rhodesiense*, whichever alternative Sir DAVID BRUCE may choose to accept as the correct answer to the question I have put to him. The parasite to which PLIMMER and BRADFORD gave the name is the parasite as it exists to-day. Personally, I think it was an adequate description, and therefore the name *T. brucei* applies to this particular trypanosome, and accordingly BLACKLOCK and I have grouped *T. brucei* with *T. evansi*. That is the first point I wish to make.

I desire to say something with regard to the important statement: "not only has the laboratory strain of *T. brucei* changed its morphology and become monomorphic, but, according to ROUBAUD, it has also lost its power of undergoing development, or even surviving in the tsetse-fly. This is not to be wondered at, as it is now nearly twenty

years since this species was first introduced into European laboratories." I should like to ask Sir DAVID BRUCE what experimental evidence he can produce in support of that statement. He says *T. brucei* has in the course of twenty years changed and become a monomorphic trypanosome. I reply that it did not change in the course of twenty years—it changed in the course of three years. The trypanosome was first discovered in 1896 by Sir DAVID BRUCE. It was not named by him; he sent it to PLIMMER and BRADFORD. In 1899, PLIMMER and BRADFORD described it as *T. brucei*. If it were dimorphic at the beginning it changed between 1896 and 1899 and became monomorphic. I say that for two reasons. In the first place, PLIMMER and BRADFORD mentioned nothing about polynuclear forms, and nothing about forms without a free flagellum. In the second place, we have slides that PLIMMER and BRADFORD made at the time, and they do not shew forms without free flagella nor with the posterior nucleus, and, moreover, we have the strain in various laboratories in this country and in Paris, and it is at the present time monomorphic. The trypanosome in 1899 was just as monomorphic as it is now.

Furthermore, I can advance another argument in favour of the statement that dimorphic trypanosomes do not necessarily become monomorphic by keeping in a laboratory. There are at the present time in the European laboratories a number of *T. equiperdum*. Recently, BLACKLOCK and I examined some four of these strains. We found three of them to be monomorphic and one dimorphic. They cannot be distinguished from *T. evansi* and from *T. rhodesiense* respectively. Two strains to which I refer at the moment were brought to Europe seven or eight years ago, and in spite of the fact that they have been kept seven or eight years by us (also in Germany), they maintain their original appearance. One strain is monomorphic and the second dimorphic.

My next point is with respect to the three groups into which Sir DAVID BRUCE has divided the pathogenic trypanosomes. Suppose we take the first group. He calls it the *T. brucei* group. I should like to ask Sir DAVID BRUCE, why *brucei*? The oldest member of that group is *T. evansi*. I should say, therefore, if we classify trypanosomes in this way the group should be called the *T. evansi* group, as this parasite was described fourteen years before *T. brucei*.

With regard to the second group. In 1910 Sir DAVID BRUCE and

his fellow-workers suddenly launched the name *T. pecorum* on the world without any adequate reason so far as I can see. I think that name is quite unjustifiable, because in 1904 BRODEN described precisely and exactly a short trypanosome, without a free flagellum, which he found in an ox. Not only does he state that no individual had a free flagellum, but he gives the length, 10·5 to 15·5 microns—a very exact description of the trypanosome. There is, therefore, even if we neglect the name *T. dimorphon*, regarding which considerable confusion exists, no reason whatever for passing over the term *T. congolense*, and the name *T. pecorum* ought to be dropped. If there is no individual rightly called *T. pecorum*, then it is obviously unjustifiable to call the second group the *T. pecorum* group.

I come to my last point. Dealing with classification as a whole, it appears to me in drawing up a classification of groups of things, one must base that classification on the variations in some definite character or characters of the group, and not one set of individuals according to one character and another set according to another character.

Let us examine the definitions of these three groups of trypanosomes. Take the first group—the so-called *brucei* group—and let us examine the definition. I approach this as a student would. “The species of trypanosomes forming this group are all more or less polymorphic, varying in shape and size from the short and stumpy, non-flagellar forms, to long and slender forms with free flagella.” The next group of trypanosomes is described as being “small and monomorphic.” The size of the members of the first group is not mentioned. The third group are “very active in their movements.” We are told nothing about the activity of the two previous groups. Groups B and C are monomorphic. How is a student to know from this description whether he is to place any monomorphic trypanosome in Group B or C? These groups are based on a number of different factors; not on the variations of one character, but on the variations of a large number of different characters.

Again in Group A “the cytoplasm contains numerous dark staining granules.” In Group B “the cytoplasm is non-granular.” Group C “the cytoplasm is clear and hyaline,” which is much the same as Group B. One cannot, by the character of the cytoplasm, distinguish between Groups B and C.

Then with regard to the micronucleus. In Group A it is "small and is situated as a rule some distance from the posterior extremity." In Group B it is "prominent, sub-terminal, and often seems to project beyond the margin." In Group C it is described as "large and terminal." Well, that is not very distinctive.

Finally, with respect to the undulating membrane. In the first group it is "well developed and thrown into bold folds." In Group B, "fairly well developed," and Group C "little developed and simple." That is not very satisfactory.

Therefore I think that this classification is not really sound from the practical point of view of the student who seeks to identify any trypanosome he may encounter.

I think it is much better for practical purposes to base the classification on some definite morphological characteristic. Dr. BLACKLOCK and I—following LAVERAN—have done this, and have taken as the three primary sub-divisions of the trypanosomes (1) those in which all individuals have a free flagellum, (2) those in which none have a free flagellum, (3) those in which some individuals have a free flagellum whilst others have not.

Classification according to behaviour in the tsetse fly, although perhaps excellent from a scientific point of view, is as a rule too complicated and difficult for the ordinary student.

Dr. A. BALFOUR: I had the privilege of being a member of the Departmental Committee on Sleeping Sickness. If I had any doubt beforehand that there was a necessity for doing something to simplify the classification of trypanosomes, that was dispelled by the meetings which took place. The whole subject was clearly in a chaotic state, and it was a very difficult thing to know where one was; hence I hailed the scheme Sir DAVID BRUCE has put forward with considerable satisfaction as far as it applied to the classification of African trypanosomes.

Dr. STEPHENS found fault with Sir DAVID BRUCE for not going into the literature of the subject fully, and dealing with the work of other observers. I can only say that I have done so, and, after doing so, my latter end was rather worse than my beginning, because I found the literature exceedingly confusing. Therefore I think that Sir DAVID BRUCE's classification is certainly a praiseworthy effort to put things on

a more simple basis. I do not, however, think that Sir DAVID BRUCE has altogether succeeded, and I would associate myself, to a certain extent, with some of the remarks of Dr. WARRINGTON YORKE, as, though Sir DAVID BRUCE's broad classification is a good one, like Dr. YORKE, I do not think one can ride rough-shod over the rules of scientific nomenclature. I am therefore at one with Dr. YORKE in thinking that in group B the name *Congolense* must stand as applied to the small monomorphic trypanosomes with no free flagella.

There are one or two other things to which I wish to refer. Dr. FANTHAM mentioned a point as regards *T. pecaui*. I at one time worked on *T. pecaui*, but unfortunately most of my records perished in a fire, and when I wrote on the subject I did so largely from memory. When Sir DAVID BRUCE visited me at Khartoum we went into the question of the Sudan trypanosomes. After comparing his specimen of *T. brucei* with mine of *T. pecaui*, I was persuaded that *T. pecaui* was what Sir DAVID BRUCE calls *T. brucei*, but I must say that this matter is still open to doubt. There is another point. On page 4 of the paper we read :—

“In regard to *T. pecaui*, there is evidently a good deal of confusion as to what is meant. It is usually described as a dimorphic species similar to *T. brucei*. ROUBAUD, however, states that it develops in the intestines and proboscis, but does not reach the salivary glands. If this is so, then *T. pecaui* cannot belong to the *T. brucei* group, but to the *T. pecorum* group.”

I should be inclined to say, “Then *T. pecaui* must be put in a separate class by itself ;” it is certainly quite unlike the *pecorum* group.

Miss ROBERTSON referred to *T. evansi*—and her memory has served her correctly, because you do get the short forms she mentioned, and it is a curious and interesting fact. They are not very common. I always had the impression I could “spot” *T. evansi* under the microscope. It is the common camel trypanosome of the Sudan, and I could at least readily distinguish it from the trypanosome of equines, namely, *T. pecaui*.

These, I think, are all the points to which I would refer. Although Sir DAVID BRUCE's classification might, and I think does, want revision in some respects, I feel he has made a praiseworthy effort to help us in a very difficult question and due credit should be given to him. I wish

it were possible, as Dr. YORKE said, to have some definite way of naming trypanosomes, not calling one after a place and another according to its morphology, and yet another after somebody's name. It would be a good thing if we could devise a definite nomenclature. We might, perhaps, call them after some one special characteristic, possibly morphological, though the difficulties are doubtless great. I hope Sir DAVID BRUCE in developing his useful scheme may be able to help us.

Dr. C. M. WENYON: I feel sure that the classification that Sir DAVID BRUCE has given us of the division of the trypanosomes into main groups according to their development in the tsetse flies, is likely to be the soundest from the zoological point of view.

I cannot agree with Dr. YORKE, who picks out a single morphological character in order to divide the trypanosomes into separate divisions. If we do that we are bound to go wrong, and I cannot help thinking that development in the tsetse fly gives a more natural classification than such a feature as the presence of a free flagellum or the absence of one. We have *T. gambiense* (which Dr. YORKE places in one group) developing in the tsetse fly in the same way as *T. rhodesiense*, which Dr. YORKE places in another group. According to Sir DAVID BRUCE's grouping these two allied forms would be grouped together along with other forms which develop in the salivary glands of the tsetse flies.

As regards morphological characters, Dr. HANSCHALL and I a year ago made extensive observations upon three strains of *T. rhodesiense*. We counted 160,000 trypanosomes in rats, with a view to finding the exact percentage of posterior nuclear forms. We found these three strains varied very much. In one strain the posterior nuclear forms sometimes rose as high as 40 per cent., while in another strain the percentage was almost uniformly 7. In others the percentage was still lower, there being 2, sometimes only 1 posterior nuclear form per thousand trypanosomes. If one was to rely upon single morphological characters, in order to separate these types, one would go astray altogether.

T. pecaui is a trypanosome which has given rise to much confusion. It was first seen by CAZALBOUI and PECAUD, and named by LAVERAN. It was later assumed that one of the trypanosomes of the Sudan must be *T. pecaui*. When STEPHENS and FANTHAM first described *T. rhodesiense*, I looked over some old films of *T. pecaui*, which I had

made in the Sudan in 1907. In them I found posterior nuclear forms as in *T. rhodesiense*, and these happened to be present in the same percentage as in the strain of *T. rhodesiense* with which STEPHENS and FANTHAM worked. It was evident that these trypanosomes of the Sudan were indistinguishable from *T. rhodesiense*, and it seems to me that if we have to abandon the name of *T. brucei* for the polymorphic trypanosome, then the name *T. pecaui* must have first place, since there is very little doubt that the *T. pecaui* of the Sudan and elsewhere is a polymorphic trypanosome, like the polymorphic *T. brucei*. It seems probable that the species *T. pecaui* was created because it was an undoubted polymorphic form which differed from the standard laboratory strain of *T. brucei* which was of the monomorphic type. A comparison of the polymorphic trypanosome with the standard *T. brucei* led LAVERAN to create the species *T. pecaui*. This comparison has again been made by STEPHENS and BLACKLOCK who have suggested the name *T. ugandæ* for this polymorphic form, though the name *T. pecaui* had already been given to this form by LAVERAN.

As regards serum tests, Sir DAVID BRUCE remarks on the impossibility of carrying out serum tests in the field, and says that they often present difficulties. Of course it would be difficult, but it does not follow that they are necessarily useless from the point of view of the separation of trypanosomes. Take an animal like the goat, which has been proved to be immune to *T. evansi* after repeated inoculations. The goat when inoculated with another trypanosome takes the infection. I think that test is of some help in the separation of trypanosomes from one another, though one must never forget that strains of one trypanosome vary very much in virulence. Sir DAVID BRUCE remarks that the main difference between *T. gambiense* and *T. brucei* is that *T. gambiense* is less virulent to small animals than *T. brucei*. Is not that in itself a kind of serum test? What real difference is there between a test of this kind and one in which an animal is used which has been made resistant artificially by previous injections of a trypanosome?

Finally, though I think that the grouping of the trypanosomes according to fly development will give us a more natural classification than one based on a single morphological character, I cannot help feeling that this classification is an impracticable one for the ordinary man in the field, who wants to be able to identify trypanosomes when he sees

them in ordinary blood films. For such a purpose, a morphological classification like that advocated by Dr. YORKE, is likely to be more useful.

Dr. G. C. Low: I do not intend to enter into the discussion in detail, but I should, however, like to ask one or two questions. It seems that a great deal of the confusion that has arisen as to the question of the original *T. brucei* is the fact of its having been, according to Sir DAVID BRUCE, originally dimorphic, although now it has become monomorphic. Dr. YORKE rather throws doubt upon its original dimorphism. I should like to ask Dr. YORKE about *T. dimorphon*. I believe it was first dimorphic and then became monomorphic.

Professor W. YORKE: The original dimorphon was sent to this country in a horse. It was possibly infected with *T. gambiense* and *vivax*. Small laboratory animals were inoculated from the horse.

Dr. G. C. Low: I now come to this point. Sir DAVID BRUCE experimentally inoculated an animal with a single monomorphic trypanosome, and the resulting infection produced both monomorphic and dimorphic forms.

Professor W. YORKE: I do not see the point.

Dr. G. C. Low: You can by inoculating the long form get dimorphism, namely, long and short forms.

Professor W. YORKE: We do not know the exact significance of the dimorphism seen in certain trypanosomes. It may depend upon the fact that individuals of different ages are of different sizes.

Dr. G. C. Low: Why should it disappear in laboratory kept animals?

Professor W. YORKE: It is not likely to disappear absolutely if the different signs represent different ages or stages in the cycle of the parasite. It is not more likely that the progeny of a single individual of a dimorphic trypanosome would be uniform in size, than that all the individuals of any human community would be all old people!

Sir DAVID BRUCE: Dr. YORKE has just told us that the original *T. dimorphon*, discovered by DUTTON and TODD, was a mixture of *T. vivax* and *T. congolense*. In my opinion it was a mixture of *T. brucei* and *T. pecorum*. If you examine the coloured plate in their original paper, which was published in Memoir XI. of the Liverpool School of Tropical Medicine, you will see that the short and stumpy, and the long and slender forms belong undoubtedly to the *T. brucei* group. The tadpole forms are probably meant for *T. pecorum*.

Professor W. YORKE: With respect to *T. vivax*. I hold that the appearance is not that of *T. brucei* or *T. gambiense*. Furthermore, about three years ago, Dr. TODD sent over to Runcorn a second pony infected with what he said was probably *T. dimorphon*. It was described by DUTTON and TODD first, and presumably they knew what they were talking about. Dr. BLACKLOCK and I worked on it and succeeded in isolating two individual trypanosomes, *congolense* and *vivax*. That is largely upon what I based my opinion that the original *T. dimorphon* was a double infection of *T. congolense* and *T. vivax*. In Africa it is exceedingly common to see such a double infection.

Dr. G. C. LOW: Going on with the question of laboratory strains of trypanosomes. There is the case of Professor LANFRANCHI in Italy, who was supposed to be working with a strain of *T. brucei* sent from Paris. He gets infected, and then it is said that the strain must have been mixed, or that *T. gambiense* must have been sent by mistake. If in Paris they keep their strains so carelessly as this, the results based on those strains must be fallacious. What can the value of such results be? This is a very important case, really, because if it was a *T. brucei* infection it is the first example of a man being experimentally infected with this trypanosome, and bears out Sir DAVID BRUCE's contention that *T. brucei* and *T. rhodesiense* are the same.

I have ceased lately to take so much interest in trypanosomes, because of the difficulties in classification, and I think it would be a very good thing if we could have some simplicity in their arrangement. It is a good principle to go on, to get a working classification, as Sir DAVID BRUCE suggests, of species, and then on little by little. Though his present classification may not be perfect, yet it is an attempt in the right

direction, and with additions and emendations I see no reason against its being adopted as a standard for the classification of African trypanosomes, pathogenic to man and his domestic animals.

Sir DAVID BRUCE: In reply to Miss ROBERTSON, in regard to the rapid change in virulence towards monkeys of *T. simiae* after passage through goats, I may say that the morphology of *T. simiae* and *T. pecorum* is sufficiently distinctive to make one quite sure that the monkey was not infected by the former and the goat with the latter species. Miss ROBERTSON has studied trypanosomes practically in the field, and, in fact, has done some of the best work in this branch of protozoology, and therefore I am glad that she agrees with the general soundness of this classification. Dr. YORKE thinks that the name of *T. brucei* should be withdrawn and the name *T. rhodesiense* substituted. This is because the present laboratory strain of *T. brucei* is monomorphic. But I have shewn again and again that the trypanosome found first in 1894, in Zululand, was a dimorphic species, and that this was the trypanosome which was sent to the Royal Society a year or two later. The description of it given by BLANDFORD, DURHAM and KANTHACK shews that it was at that time a dimorphic species, and if it has become monomorphic now, that must be due to the artificial conditions of a laboratory. I have also shewn that a dimorphic trypanosome in Nyasaland, after some thirty passages through white rats, became monomorphic.

It is, therefore, quite possible that the originally dimorphic *T. brucei* may have become monomorphic by its long sojourn under laboratory conditions. What is certain is that the trypanosome discovered in Zululand in 1894, and described as the cause of Nagana, was morphologically identical with the trypanosome obtained from the same place in 1913. and that both are morphologically identical with the trypanosome obtained from Rhodesia and Nyasaland, and called *T. rhodesiense* by STEPHENS and FANTHAM.

Dr. YORKE has placed *T. evansi* in a monomorphic group, but I think he is wrong in this, as *T. evansi* undoubtedly does shew a few short and stumpy forms, and should therefore be placed in the dimorphic group.

T. evansi also has been studied in old-established laboratory strains,

and if studied in the field might shew that life in a laboratory for countless generations has also modified its morphology.

Dr. YORKE also asks what experimental evidence I can produce in support of the statement that "not only has the laboratory strain of *T. brucei* changed its morphology and become monomorphic, but according to ROUBAUD it has also lost its power of undergoing development, or even surviving in the tsetse fly." In the first place I sent home to England in 1896 a dimorphic trypanosome which is now stated to be monomorphic; and in the second, ROUBAUD took a laboratory strain of *T. brucei* to West Africa, and found that it would not pass through the usual cycle of development in the tsetse fly.

Dr. YORKE also says that he has lately examined four or five laboratory strains of *T. equiperdum*, and that some are dimorphic and some monomorphic. All I can say is, that if he perseveres in the examination, description and renaming of old laboratory strains of trypanosomes, he will add to the present confusion of classification and not help in bringing order into it, which we all desire. Who can tell what a trypanosome is, after it has passed through the vicissitudes and accidents of ten or twenty years of laboratory life?

Dr. YORKE says that *T. evansi* was named fourteen years before *T. brucei*. But even in 1895, when I was working in Nagana, LINGARD in India believed that *T. evansi* was the common rat trypanosome, and that horses became infected by eating corn soiled by rats. I named the first group the *T. brucei* group, because *T. brucei* is the best known of the African dimorphic type of trypanosomes, and that infinitely more work has been spent on it than any other, and that we really do not know much about *T. evansi*, except from the study of laboratory strains. MITZMAIN and others are remedying this.

Dr. BALFOUR thinks that Group B, with the name *T. congolense*, must stand in connection with the short monomorphic trypanosome without free flagellum. For my part, I think that *T. dimorphon* (LAVERAN and MESNIL) is the same as *T. congolense*, and therefore from the point of view of priority the group should be called the *T. dimorphon* group, and not the *T. congolense* group. When I described the central and the eastern African type of this monomorphic form, I was altogether ignorant of the west coast types, and I could find no adequate description of them. I therefore called the eastern type *T. pecorum* (sp. nov.), and

in this I have been confirmed by LAVERAN and MESNIL, and by other workers.

In regard to *T. pecaudi*, it is evident that different workers have been calling different species by that name. We must therefore await more knowledge before we can decide to what group it belongs.

Dr. F. M. SANDWICH: This subject of trypanosomiasis is always fascinating. Dr. BAGSHAWE has enlightened us upon several occasions, but I do not think we have ever had a more interesting or a more lively discussion than this evening. It is a comfort that there are some papers we have not yet read, and I am sure that those who read this discussion will learn a great deal.

Our very best thanks are due to Sir DAVID BRUCE for coming here at a time of stress to enlighten us, and he certainly has enlightened us, and he has opened the way to future investigation. I think, in thanking him, we ought to invite him to take home with him our admiration for the beautiful drawings signed by a lady artist not unknown to our Fellows. Lady BRUCE is always working, always modest, and always to be admired.

NOTES AND COMMENTS.

THYMO-BENZOL IN BILHARZIASIS.

BY

WILLIAM ROBERTSON, M.D.

For some months I have been using thymo-benzol as a bilharzia-toxin, and with very satisfactory results. I may say that even in the worst cases all symptoms and signs of the infection disappear. An egg or two may be discovered, after prolonged search, in cases otherwise apparently free and well.

The following points may be noted :—

1. All ureteral, vesical, and urethral pain disappears.
2. Hæmorrhage ceases.
3. In two to three days, after 5i doses of benzol (pure), the ova come off, mostly stained black, with some of normal colour, but all dead. They will not hatch out.
4. The detritus of bilharzia disappears, and the exudate in the urine on boiling disappears to a thin haze, or is absent.
5. The remedy is evidently “anti” to the helminth toxin. These toxins are responsible for headache, frequent sweating, giddiness, pallour, and emaciation. All these disappear under the remedy. Frequent micturition and backache also disappear. At first I gave benzol (pure), but I have since considered gr.3 thymol in $3\frac{1}{2}$ benzol 4tis horis equally good.

I have observed no poisonous symptoms from the remedy. I have now used the remedy interruptedly, giving in the intervals urotropine. I have also found that secondary infections disappear soon. I have only met with urinary schistomiasis, but imagine, from its presence in the fæces also, that it will serve in intestinal bilharzias cases.

I look upon the disappearance of constitutional symptoms as evidence of the powerful action of the remedy on the worms themselves, and that in time it will kill them.

LIBRARY NOTES.

Under this heading we propose to review recently published works sent us for that purpose, and a short notice of any other works presented to the Library.

REVIEW.

Tropical Hygiene for Anglo-Indians and Indians. By the Hon. Surgeon-General Sir PARDEY LUKIS and Major R. J. BLACKHAM, C.I.E., R.A.M.C. W. Walker & Co. Price 4s. 6d. net. Second Edition.

This small volume of 270 pages, which now appears in a second edition, is a most useful guide on Tropical Hygiene for those to whom it is addressed. It does not profess to be a manual of tropical diseases, and only refers to these in order to indicate the measures which would be taken for their prevention. The chapter on insects and disease in the tropics is a particularly useful one, as it not only refers to mosquitoes and other insects which are the carriers of general diseases, but also describes many body parasites which are a particular nuisance. Clothing, food, water supply and disinfection are carefully dealt with, as well as the disposal of the excreta. We are glad to notice, under the head of Water Supply, that filters are condemned, but we cannot help a feeling of doubt as to the wisdom of trusting to the use of permanganate of potash for the purification of wells contaminated by cholera. It would be a great pity if this were regarded in any way as a substitute for boiling. However, the book is a most useful one, and we cordially commend it.

Obituary.

HENRY SHERWOOD RANKEN, CAPTAIN R.A.M.C., V.C., M.B.,
Ch.B. (GLAS.), M.R.C.P. (LOND.).

The Society has to mourn the loss of Captain HENRY SHERWOOD RANKEN, who died at Braisne, in France, on September 25th, as a result of wounds received on the 21st of that month.

Captain RANKEN was the son of the Rev. Henry Ranken, minister of the parish of Irvine, Ayrshire, and was born in 1883. He received his medical education at the University of Glasgow, where he graduated M.B., Ch.B., with commendation in 1905; and that he was highly esteemed by his teachers there, is shown by the fact that he was appointed house-physician and house-surgeon to the Western Infirmary, Glasgow. At a later date he acted as assistant medical officer to the Brook Fever Hospital, London. In 1909, he entered the Royal Army Medical Corps, and shewed himself keenly interested in bacteriology, and more especially in the problems presented by tropical medicine. He took 'first place at the entrance examination, gained the Tulloch medal, the medal for military medicine, the medal and prize for tropical medicine, the De Chaumont prize in hygiene, and the prize of £20 for grand aggregate marks in all examinations during the probationary course, open to the Royal Army Medical Corps and the Indian Medical Service. His bent was towards research. He worked with Sir William Leishman, and also assisted Mr. H. G. Plimmer in his investigations on the experimental treatment of trypanosomiasis. Mr. Plimmer was wont to testify to his zeal, enthusiasm and carefulness.

In 1910, Captain RANKEN became a member of the Royal College of Physicians of London, and finally entered the Egyptian Army, being selected by the late Colonel H. B. Mathias for special work in connection with sleeping sickness. He was made a member of the Sudan Sleeping Sickness Commission and sent to the remote station of Yei, in what was, until recently, the Lado Enclave, and is now known as Western Mongalla. In the sleeping sickness camp there he was made responsible for the treatment of patients, and was soon busy testing the effects of various new remedies, and more especially of salvarsan and metallic

antimony. He worked under considerable difficulties, but he had the dour strain of the Scot in him, and laboured indefatigably.

Further, he arranged and equipped a little laboratory where he spent many hours of research in connection both with sleeping sickness and yaws.

His native patients, of many tribes and speaking many dialects, liked and trusted him. He learned to converse with some of them in their own tongues, and soon gained their confidence.

Though so far from any medical centre and from sources of information, his pen was by no means idle. Considering his age, his contributions to the literature were considerable, and were all characterised by care and accuracy. They were as follows:—

“Reports on Experimental Treatment of Trypanosomiasis.” (With H. G. Plimmer and W. B. Fry). *Proceedings of the Royal Society*, 1910-11.

“A Note on ‘Granule-Shedding’ in *Treponema pertenue*.” *British Medical Journal*, June 29th, 1912.

“Note on the Occurrence of a Spirochæte in *Cercopithecus ruber*.” *British Medical Journal*, June 29th, 1912.

“Further Researches on the Extrusion of Granules by Trypanosomes, and on their further Development.” (Fry, Ranken and Plimmer). *Proceedings of the Royal Society*, Series B. Vol. 86, 1913. Also *Journal of the Royal Army Medical Corps*. Vol. 21. No. 2. August, 1913.

“A Preliminary Report on the Treatment of Human Trypanosomiasis and Yaws with Metallic Antimony.” (Plimmer). *Proceedings of the Royal Society*, Series B. Vol. 86, 1913. Also *Journal of the Royal Army Medical Corps*. Vol. 21. No. 3. September, 1913.

At Yei, he found the *Sleeping Sickness Bulletins*, and later the *Bulletin of the Tropical Diseases Bureau* invaluable, and was always glad when the post runners brought in a new number. Captain RANKEN was a great favourite with all who knew him. He was modest and unassuming, but he had a fund of quiet humour, and a most kindly and generous nature. The writer will not readily forget the hospitality shewn him and Colonel Mathias at Yei in 1912, both by Captain RANKEN and his brother officer, Captain R. J. C. Thompson. As we met in the forest, some miles from the post, two of us, with one accord,

raised our helmets and exclaimed, "Dr. Livingstone, I presume!" having, unknown to each other, determined to employ this historic greeting. One recalls how Captain RANKEN laughed heartily over this little episode.

At Yei, there was a special *Glossina palpalis* which used to lie in wait for the traveller at the ferry across the river, and follow him for a mile or so through the cleared area. Captain RANKEN had a special nickname for this fly, which was exceedingly wary and always evaded capture. He was a keen shikari, and every year succeeded in obtaining his two elephants, but he was a good sportsman and never allowed his work to suffer by reason of his love for the chase.

He died gallantly and nobly, serving his country, doing his duty fearlessly, and as a result of tending, under fire, the wounded committed to his care. His loss is a grievous one to the cause of tropical medicine, for good research workers are few. He was on leave at the time the war broke out, and, having volunteered, was amongst the first of his distinguished Corps to go to the front.

The following extract from a private letter which we have been privileged to reproduce tells of Captain RANKEN's heroism and devotion:—

"Only last night I amputated poor RANKEN's leg above the knee-joint—a terrible shell wound it was—but he will probably get a V.C. for his behaviour. Although the leg was only hanging on by very little he continued to dress his wounded in the firing line."

Captain RANKEN was mentioned in despatches, and was also the recipient of the Croix de Chevalier of the Legion of Honour, and more recently was awarded the V.C., being included in the first list of those who received this unique distinction. Unfortunately his death occurred before these honours could be conferred upon him.

The Society has lost a valued Fellow, but he has left behind him a record of work well, faithfully and bravely accomplished even unto the end.

A. B.

TRANSACTIONS
OF THE
SOCIETY OF TROPICAL MEDICINE
AND HYGIENE.

DECEMBER, 1914.

VOLUME VIII. No. 2.

Proceedings of a Meeting of the Society on Friday, November 20th, 1914.

SURGEON-GENERAL

SIR R. HAVELOCK CHARLES, G.C.V.O., I.M.S.(R.), *President*,
in the Chair.

THE WAR AND TYPHOID FEVER.

BY

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I.

From the days of Homer, Apollo, the far darter, has been a much more formidable foe than his colleague Mars. With the two in conjunction unspeakable woes afflict the sons of men. In his great strait David, you remember, chose three days of pestilence as the equivalent of three months' military disaster. To-day the front of Mars is wrinkled, the world is at war, and the problem for the children of Aesculapius is to keep grandfather Apollo from taking a hand in the fray. In this game another member of the family, Hygeia, holds the trump card and gives victory to the nation that can keep a succession of healthily efficient men in the field. The Empire is confronted with a great task, in the successful performance of which the medical pro-

fession may, play a leading part. For generations the health of the army and navy has engaged the attention of the very ablest men in our ranks. Let me quote a sentence written in 1785 by GILBERT BLANE, a pioneer in sanitation, and as true to-day: "The great importance of the subject (that is, prevention) will plead my excuse for again calling to mind that such attentions are not only dictated by humanity, but would be the greatest wisdom in an economical and national light, considering how expensive it is to *replace* men and to support invalids, not to mention that it is upon the health and lives of men that every public exertion essentially depends, and upon which even the character of officers in the day of battle may depend."¹

Of the camp diseases, typhus, malaria, cholera, dysentery, and typhoid fever, it is a reasonable hope that the armies of the West will escape the first three. Dysentery is pretty sure to cause trouble; but with regard to enteric fever we are on trial as a nation and as a profession, in what way it will be the object of this address to shew.

The nineteenth century saw the discovery of the cause of typhoid fever, the recognition of its transmission through polluted water or milk, and the enforcement of sanitary measures, which have caused a steady and gratifying reduction in its prevalence. Those of us brought up upon the writings of SIMON, BUCHANAN, BUDD, and MURCHISON, and convinced of the truth of the water-borne and milk-borne theories, were often confronted with epidemics in schools and barracks and private houses in which it was not possible to trace the infection to either of these sources. Yet experience lent little support to a doctrine of direct contagion. There was some other factor. Even with the purest supply of water and of milk, cases would crop up and local outbreaks occurred. Within the past ten or fifteen years we have not only filled gaps in the etiological picture, but we have added so many details that the canvas is approaching completion. Let me dwell upon four points in our new knowledge.

I. THE IMPORTANCE OF THE INDIVIDUAL CASE AS A FACTOR IN INFECTION.

Though the infectiveness was recognised, only within the past decade have clinicians made it an essential feature to completely sterilize the dejecta, urine and fæces, and to avoid all possible contamination about the patient. As in surgery, we have changed the antiseptic to an aseptic

battle, and nowadays the physician feels as keen a duty to keep the surroundings of a patient sterile as to treat his symptoms.

This in itself is a great gain, as the possibility of the abolition of the disease is a problem of the sterilization of the individual cases as they occur. I cannot here enter into the question of the methods of conveyance, but it is sufficient to say we have recognised fingers and flies as two of the chief, and the special liability in houses and wards of food contamination.

II. RECOGNITION OF THE PROTEAN CHARACTER OF THE DISEASE.

Not only are there differences in the germ that causes typhoid, but the clinical picture itself varies from the text-book standard very much more than was dreamt of by LOUIS, BUDD, FLINT, or MURCHISON. A transient febrile attack, a slight diarrhoea, bronchitis, acute nephritis, an attack of pneumonia, cholecystitis, acute pyelocystitis, may be a manifestation of the infection. In endemic areas mild, indefinite illness in children may be due to the typhoid bacillus. The organism, indeed, may lodge and live in an individual without ever causing symptoms, and then acutely excite an illness without a trace of resemblance to the disease we usually associate with its name. One of the first cases in which this was recognised I saw with Dr. CUSHING in Dr. HALSTED'S wards—a woman, aged 26, who had a clean bill of health except for occasional attacks of abdominal pain and vomiting. It was evident at the time of examination that she had acute cholecystitis. Dr. CUSHING removed fifteen large gall stones; pure cultures of the typhoid bacillus were isolated from the mucous contents of the bladder. Here was a woman who had never had, so far as could be ascertained, typhoid fever, and yet she had probably had for years the organism in her gall bladder, which had ultimately caused the formation of the stones. This case at the time unique, is no longer so. In the Spanish-American war, and in the South African war, there were an extraordinary number of mild ambulatory cases, which in the former were frequently reported as malaria. In public health work it is all-important to recognise these mild atypical cases. Dr. CHALMERS, in the Health Report of the City of Glasgow for 1913, calls attention to the simulation of enteric by mild pneumonia and by intestinal catarrh.

Eight cases of enteric appear to have originated from an undetermined case of the latter in a child.

III. THE DISCOVERY OF TYPHOID CARRIERS.

Briefly stated, in from 1 to 3 per cent. of cases of enteric fever the bacilli do not disappear from stools or urine. The patient becomes a chronic carrier and a possible menace to the community. It has been estimated that, in countries in which typhoid fever prevails, the typhoid carriers number from 2 to 3 per 1,000. Infectivity may exist for years, and scores of small epidemics have been traced to carriers. How persistent the infection may be, and how difficult to get rid of, is well illustrated by the case studied for the past five or six years by DAVIES and WALKER HALL, of Bristol. The patient had enteric in July, 1905, and eight instances of infection had been traced to her. The special interest in the case is the careful study of the different plans of treatment and the variability of the presence of the organisms in the urine. They were also isolated from her blood five years after the original attack.² The relation of the carrier to public health is of vital importance, particularly the question of the detention of notorious carriers who follow dangerous occupations. The New York Board of Health was judged to be within its rights when an action was brought against them for the illegal detention for three years of the celebrated "Typhoid Mary." Carriers should not follow the occupation of cooks, butchers, grocers, as the fingers deposit bacilli on everything they touch, unless scrupulous attention is paid to cleanliness after defæcation. The good effect of precautionary measures in the case of chronic carriers is illustrated by the report of LENTZ from the Oberstein district.³ For ten years the disease had been endemic, and then a systematic attempt was made to discover the carriers, of whom six were found in 1894, two in 1897, and one in 1898. They were practically all mothers with large families. It was impossible to enforce vigorous methods of isolation, so that repeated warnings were given, and instructions as to scrupulous cleanliness, particularly after defæcation, never to touch an article of food without a systematic washing of the hands, and having their under-linen carefully sterilized. The fever in the district has practically disappeared.

IV. IMMUNISATION.

Lastly, and the most important point of all, is the discovery of immunisation against the disease, for which we are indebted to the brilliant investigations of Sir ALMROTH WRIGHT. The net result of the enormous amount of work which has been done since the publication of his first paper—September, 1896—is that, for a time at least, man may be immunised safely and surely. It is only by the statistical method that we are able to judge of the results of the practice. While in a way this is unfortunate, as figures have an extraordinary mobility as manipulated by different individuals, still, practical men have to use them and to form judgments by their help. The new iatro-mathematical school of KARL PEARSON and his scholars have made the profession cautious in drawing results from statistics; but in the matter under consideration the figures are, I believe, trustworthy. I will only give a few, the more important.

For many years the death-rate from typhoid fever in the United States has been very high. The disease prevails widely in the country districts. During 1912 it was 16·5 per 100,000 of the population—the lowest for many years. Antityphoid inoculation was voluntary in the U.S. army from 1909 to part of 1911; it was made compulsory in part of 1911 and in 1912 and 1913. Major RUSSELL's last report, dated May 2nd, 1914,⁴ gives the following figures:—

Typhoid Fever, 1907 to 1913, for the whole Army, Officers and Enlisted Men, American and Native Troops.

Year.	Mean Strength.	Cases.		Deaths.		Per-centage of Total Cases.	Occurring among those who were Vaccinated.	
		No.	Ratio per 1,000 of Mean Strength.	N.	Ratio per 1,000 of Mean Strength.		Cases.	Deaths.
1907	62,523	237	3·79	19	0·30	8·0	—	—
1908	74,692	339	3·20	24	0·31	10·0	—	—
1909	84,077	282	3·35	22	0·26	7·8	1	0
1910	81,484	198	2·43	14	0·17	7·1	7	0
1911	82,802	70	0·85	8	0·10	11·4	11	1
1912	88,478	27	0·31	4	0·044	14·8	8	0
1913	90,646	3	0·03	0	0·0	0·0	1	0

Major RUSSELL states that no harmful effects have been produced. The newspaper reports of death following antityphoid inoculation in the United States have been shewn to be erroneous. In the case of Private Pantzer, of the National Guard, Brooklyn, death was shewn to be due to malignant endocarditis, and in no way the result of inoculation.⁵ The value of these results must be taken in connection with the fact that in many places the barracks are situated in districts in which typhoid fever prevails. In 1911 and 1912 there was a concentration of many thousands of United States troops on the Mexican border in localities quite as favourable to the spread of enteric as in the Spanish-American war.

Apart from vaccination, there has been in all armies a reduction in the number of cases of typhoid fever; thus, between 1882 and 1909 the incidence of the Prussian army dropped from 6·7 per 1,000 to 0·4, while in the same years in the French army a reduction from 16·6 to 3·4. But the special value of the experience of the American army is the remarkable drop in the case incidence which followed antityphoid inoculation without special change in the sanitary environment of the troops. An interesting comparison is reported⁶ of two divisions stationed in nearly the same latitude for about the same length of time each on a good site, with artesian water of unimpeachable purity. In the one at Jacksonville, Florida, in 1892, among 10,759 men there were 1,729 certain cases, probably 2,693 (the question of diagnosis of typho-malaria, etc.), with 288 deaths. In San Antonio, Texas, in 1911, among 12,659 men, all inoculated, there was one case of typhoid fever, and no death. In France the results appear to be equally satisfactory, and there is no country in which measures of protection are more needed, as during the past twenty years among the French troops in France there have been 66,000 cases, with 10,000 deaths.⁷ Professor VINCENT reported to the International Medical Congress last year that among 30,325 vaccinated men no case occurred, while in the unvaccinated the case-rate was 2·22 per 1,000 in the metropolitan troops and 6·34 in the colonial. Specially good results have been met with in Algiers and Morocco, where the inoculation is compulsory, and the incidence per 1,000 has fallen from 15 to 5. A striking illustration is reported from Avignon by PAGET, in a recently issued Research Defence Society pamphlet. Out of 2,053 men 1,366 were protected and 687 were not. The non-protected had 155

cases with 21 deaths; the protected had not a case. The Italian experience in Tripoli shews that the incidence of the disease among the unvaccinated was 35·3 per 1,000, while among the vaccinated the incidence for those inoculated once was 1·34 per 1,000, for those inoculated twice 1·65, and for those inoculated three times 0·49. The most careful study of the statistics for the British army are those presented in the report of the Antityphoid Committee, 1912:—"The histories, as regards typhoid fever, of 19,314 soldiers, whose average period of service abroad was twenty months, were carefully followed, and every precaution possible was taken to verify the diagnosis bacteriologically. Of this number 10,378 were inoculated and 8,936 not inoculated. The case incidence of typhoid fever among the inoculated was 5·39 per mille, and among the non-inoculated 30·4 per mille.

"There is no reason for supposing that this difference can be attributed to a want of homogeneity between the two groups. The age distribution among inoculated and non-inoculated was approximately the same. They were intermingled and lived under identical conditions."

The profession is greatly indebted to Sir WILLIAM LEISHMAN and his colleagues, HARRISON, SMALLMAN, and TULLOCK, for the good work they have done in connection with this subject.

SYMPTOMS FOLLOWING INOCULATION.

As in this country the practice is voluntary, and as in certain quarters opposition has been offered, I have thought it well to collect data of any untoward effects, and I have to thank many correspondents who have replied to my note in the *British Medical Journal* of October 10th. In the first place it may be stated that with ordinary care and precautions large bodies of troops may be successfully inoculated with extraordinarily little discomfort or disability. Colonel HODGETTS has kindly given me the figures of the recent inoculations of the Canadian contingent, some 31,000 strong, made under his supervision in the camp at Valcartier in the Province of Quebec. Of the total number only one had a local abscess at the site of injection, and there were no serious sequelæ. This may be said to be an exceptionally good record. The inoculations in this country during the past three months have been on a larger scale than ever before attempted, and considering the enormous number—several

hundred thousand—the serious sequelæ have been very few. We may group the symptoms as follows :—

1. A varying proportion no symptoms, other than a little headache or malaise, with slight redness and swelling at the point of inoculation.
2. A large proportion run a normal course of what may be called the inoculation fever, which has many resemblances to the so-called serum sickness. The temperature rises within ten or twelve hours, sometimes with a slight feeling of chilliness, and vomiting may occur. There are headache, fugitive pains in the back and joints, sometimes abdominal tenderness, and for twenty-four or thirty-six hours the patient may feel very badly. In mild forms the temperature rises to 101° or 102° ; in the more severe to 103° and 104° , or even higher. Sometimes there is diarrhoea; in other cases, perhaps in the majority, there is constipation. Giddiness and fainting are reported, and one physician within the first ten days had curious nervous symptoms, feelings of apprehension, and a transient state of neurasthenia. He felt inability to control his muscles, and dreaded lest he should be unable to avoid some impulsive act. There was a slight mental disturbance, and he had what he called “dreadful feelings,” and had difficulty in forcing himself to do the simplest acts. In the North Midland Division, among nearly 16,000 inoculated, a man, two days after inoculation, had marked mental symptoms suggestive of confusional insanity, which, fortunately passed away. I saw with Dr. COLLIER, an officer whose case was very fully reported to us by Dr. JOYCE of the 4th Royal Berkshire Regiment. He was inoculated on September 14th and, after the usual slight local and general symptoms, on the 17th the temperature was normal. On the 18th he had giddiness, and on returning to his billet when the door was opened he mistook the parlourmaid for the colonel, and raising his hand to the salute overbalanced and fell unconscious. He had a few days' leave, and some weeks later had several giddy attacks.

Heavy exertion and exposure within twenty-four hours after inoculation may be followed by sharp general symptoms. In connection with the abdominal pains that may occur, it is interesting to note that Professor BOYD of Winnipeg, now associated with the 3rd North Midland Field Ambulance, reports two cases (admitted on the same day) with appendicitis—one on the third day after inoculation, the other within twenty-four hours. Both had acute perforation. There

have been several reports of sharp localised pain in the region of the caecum, with slight diarrhoea. The highest temperature recorded in the notes sent to me (Professor BOYD) was $106\cdot4^{\circ}$, four days after inoculation.

In what may be called the normal course there is oedema and redness at the site of inoculation varying in extent, and several correspondents have noted a curious migration of the erythema downwards towards the elbow, and even reaching to the wrist. Blotchy erythema may occur about the joints, and purpura has been noted.

CASES WITH UNTOWARD EFFECTS, LOCAL OR GENERAL.

(a) *Locally*, the redness, swelling, tenderness rarely persists for more than a day or two, and may be equally marked at both inoculations, or may be slight at the first and abundant at the second, or *vice versa*. The local process may go on to suppuration. How rare this is may be judged from the experiences of the Canadian contingent already referred to, in which only one abscess occurred among some 31,000 cases. This is, indeed, a remarkable record, so I doubt if there is any hospital in the kingdom in which during a year's experience abscess does not follow some form of hypodermic injection. I have had no report of severe sepsis following the local abscess.' Lance-Corporal Goatley, whose case has been exploited by the "antis," had a septic wound, which proved, on investigation by Surgeon-General WHITEHEAD, to be an abscess following ordinary vaccination for small-pox, and the report states that the bad arm directly followed from his own neglect. And I may state that he was not discharged from the army for ill-health due to the vaccination.

(b) *General*.—The inoculation fever and its symptoms rarely last more than a couple of days; but in a few cases unpleasant, or even serious, complications may follow.

With the fever there may be pains in the joints, superficial redness, and even effusion. A patient was admitted to the base hospital, Oxford, with effusion in the left knee, following antityphoid inoculation three weeks previously. It resembled a gonorrhœal synovitis, but there was no urethral discharge. I have already referred to the abdominal pains on pressure in the caecum region and the coincidence of appendicitis in two cases. Jaundice has been noticed in a few instances. There

were four in the North Midland Division, coming on about a week after inoculation (BOYD). Symptoms suggestive of enteric, and enteric itself, may follow inoculation.

Dr. WALTER BROADBENT, of Brighton, sends a report of a case: 'Second inoculation on October 13th, followed by headache and pains in the limbs on the 14th, then fairly well until the 20th, when he had headache, a temperature of 103.4° ; on the 21st the temperature ranged from 101° to 102° , on the 22nd from 98.6° to 102° , then gradually fell to normal. On the 26th the tongue was very furred, there were no spots, but there was a positive Widal reaction on the 24th. The case was not treated as enteric.

In a case, the notes of which were sent by BOYD, the second dose, given on October 16th, was followed by sickness and giddiness. On October 19th and 20th he had diarrhoea, for which he saw the regimental medical officer. On October 23rd he was seen by the surgeon of the 1st North Midland Field Ambulance, who found him with a temperature of 101.5° , constipation, rose spots, slight abdominal tenderness, large spleen. After consultation, it was decided that it was a typical typhoid case, and he was sent to the 2nd General Hospital, London.

Occasionally septic fever follows unassociated with the local lesion. A case of this type, under the care of Colonel HOOD and Dr. HOBHOUSE at Brighton, I had the privilege of seeing at the height of his illness. I am indebted to Dr. HOBHOUSE for the notes:—

On October 23rd I saw at Brighton, with Dr. HOBHOUSE and Dr. HOOD, Private Walter Fuller, aged 23, No. 8 Bedfordshires, who had his first inoculation on October 3rd. Slight headache on the 4th, with fugitive pains, but he did not feel badly until the 7th, when there were fever and pains in the joints. On admission to hospital on the 9th the temperature was 102.5° . On the 11th his temperature was 104° , much pain, particularly in the joints, slight swelling and redness of the ankles and the smaller joints of the hands, with great stiffness and inability to use the muscles. On the 17th he began to have pain in the chest, with signs of involvement of the right base. On the 18th the leucocyte count was 15,300 per cubic millimetre, the pains in the chest were worst, he had cough, and the consolidation in the right lower lobe had increased. The Widal reaction was markedly positive. Between the 16th and the 23rd the temperature rose to about 103° each

day, there were pain and swelling in the joints, redness over the ankles and knuckles, and much disability. When I saw him on the 23rd he looked very ill, the respirations were 40, pulse 100, the small joints of both hands shewed swelling with slight erythema, tenderness on pressure and on movement, redness over the left ankle, moderate effusion in the left knee-joint and right elbow, consolidation of the right lower lobe, and left pleural effusion reaching to the fourth rib in front. The heart sounds were clear; the spleen was not palpable. There was no redness or swelling at the site of inoculation. The patient remained very ill for the following week, although the temperature was lower, rarely going much above 102° . There was a to-and-fro pericardial murmur. The patient then began to improve, and on October 30th the temperature for the first time fell to 99° . Between October 30th and November 5th it fluctuated around 100.5° , and then fell to normal. The smaller joints remained painful, and it was not until November 11th that he began to use his hands and arms. He is now convalescent.

In the same ward I saw, with Dr. HOBHOUSE, a man with dermatitis in the region of one axilla, which had spread rapidly after inoculation. He had symptoms suggestive of peripheral neuritis, stiffness of the arms, and loss of the knee-jerks. He had had zinc ointment used for a very large area, which Dr. HOBHOUSE thought might possibly be the cause of the neuritis.

The importance of avoiding exposure for a day or two after inoculation is emphasised by the fact that cases of pneumonia have been reported by several observers. In the North Midland Division series, among nearly 16,000 instances, in two cases lobar pneumonia followed within twenty-four hours (BOYD). Pneumococci were present in the sputum in both cases.

Private G. B. Jones, 12th Sherwood Foresters, reported by Dr. WALTER BROADBENT, was inoculated October 6th; chill on the 7th, and on the 8th was admitted to the 2nd General Eastern Hospital with pneumonia of the middle and lower lobes on the right side, and the lower lobe on the left, with a temperature of 103° , pulse 120, and much delirium. He had a very severe illness, and died on October 14th.

Reports of death as a result of the inoculation are false. Dr. SELBY wrote from Aldershot (October 17th, 1914):—

This morning I was trying to persuade my Kitchener army men to be inoculated, when I was confronted by one man who said he went down to Shorncliffe last week-end and that there they had told him that three men had died within twenty-four hours of inoculation.

I wrote to Colonel WILSON, who replied (October 21st, 1914) that there had been no death from this cause, and giving particulars of the fatal cases from accident or disease since the formation of the camp.

The Beaujon Hospital nurse, Paris, whose case is so often quoted, died of typhoid fever a month after the last inoculation. She might very possibly have contracted the disease previously. The Neckar Hospital nurse received therapeutic injections of typhoid serum during the course of the disease, not a protective inoculation.

Private Pantzer of the National Guard, Brooklyn, died of malignant endocarditis and the inoculation had nothing to do with his fatal illness.⁸

II.

Perhaps the best chapter in British sanitation is that which deals with typhoid fever. While a decrease in the incidence of the disease has been more or less general throughout civilised countries, nowhere else has the fall been so progressive and striking. Twenty years ago the death-rate per 1,000,000 of inhabitants was about 300; in 1912 it had fallen to 44, the lowest ever recorded; indeed, up to 1904 the rate had never fallen below 100. Enteric fever may be said to be in its "last ditch," but that it is still putting up a strong fight is indicated by 1,600 deaths in England and Wales in 1912. It prevails less in London than in the Midlands and in the South, and is much more frequent in the North, in both urban and rural districts. In certain urban districts the highest case-rate per 100,000 of the population was 34. In many of the large cities in the North, as in Liverpool and Glasgow, in which the disease was very prevalent, the fall has been progressive and rapid. In the former city in 1895 there were 1,300 cases. In 1911 it had fallen below 200. In Glasgow the case-rate per 1,000,000 has fallen from 1,386 in 1891 to 232 in 1913, and the death-rate per 1,000,000 from 218 in 1891 to 36 in 1913. General betterment of sanitation, particularly improved housing, better diagnosis,

greater care of the individual cases—to these factors may be attributed a large part of this decrease. But there is another to which the attention of the medical officers of health has been strongly directed—namely, the removal of local sources of infection by the isolation of the sick in hospitals,⁹ in which in some cities the proportion of cases treated has risen from 30 or 40 per cent. to 80 and 90. It has been well said that enteric fever is the sanitary index of a country; and that to-day our camps are not hotbeds of the disease is the result of more than half a century of intelligent and efficient sanitation.

Neither the profession nor the people at large appreciate fully the extraordinary sanitary advantages enjoyed by this country. In medical practice, if I were asked to state the most striking difference between England and the United States and Canada, I should say the absence of enteric fever in hospital and private work. The tragedy of typhoid fever was ever present, and one felt constantly outraged at the wantonness of the sacrifice. In full measure the tragedy was brought home to the United States during the Spanish-American war. There never has been in history a campaign so fatal to an army not yet in the field. Listen for a moment to the story of what may happen after mobilisation in a typhoid ridden country. Returning to the United States from a visit to England in the autumn of 1898, I found but one subject engaging the attention of the profession—the appalling outbreak of typhoid fever in the volunteer army, distributed in seven camps in different parts of the country. The figures published by REED, VAUGHAN and SHAKESPEARE in their elaborate report, of which a good epitome is given by Dr. CHRISTOPHER CHILDS¹⁰ shew that in six months, among 107,973 men, there were 23,738 cases of typhoid fever and 1,580 deaths. At Camp Alger, near Washington, with a mean strength of 21,988 men, there were 1,951 cases of typhoid fever. Never have I seen so many cases of fever concentrated together, barrack after barrack filled with the victims of neglected sanitary precautions. The lesson drawn by the authors of the report on this epidemic was that the disease was not water-borne, but that nearly two-thirds of the cases were examples of “connectible attacks”—that is, due to infection within the tent or from adjacent tents. It was the first great epidemic to call attention to the importance of local infection by means of fingers, food and flies. Two other points

were brought out—the frequency with which erroneous diagnosis was made, particularly in the southern camps, where many cases were supposed to be malaria; and the large number of minor attacks indicated by nothing more than transient malaise, slight fever, or a gastro-intestinal attack.

RECOMMENDATIONS.

More than three months have passed, and the reports from the camps indicate that nowhere is typhoid fever prevalent. That isolated cases have occurred should make the medical officers of health and the military surgeons redouble their efforts to prevent the spread. These should be watched with the utmost care, since, as Dr. CHILDS points out, epidemics in camps are usually preceded by scattered cases or by the unusual prevalence of diarrhoea. *Watch the common ailments.* should be the motto of the camp surgeons. The following measures are indicated :—

1. Every recruit should be asked whether he has had typhoid fever, or if during the previous twelve months he has lived in a house with a case of fever. An affirmative answer should mark the man for laboratory study. This may seem an irksome precaution, but in preventive medicine nothing necessary is irksome.

2. A realisation of the extremely protean character of typhoid fever, so that mild cases of enteritis, obscure forms of bronchitis and pneumonia, and mild cases of fever should be watched with care.

3. Every typhoid patient should be regarded as a focus of infection, and should be suspected as long as the bacilli are present in the discharges. The cases should not be treated in the general wards with other cases. Measures should be taken in the larger camps and in the garrison towns to segregate the cases.

4. No typhoid patient should receive a clean bill of health until he has been shewn by bacteriological examination to be harmless.

5. Ample provision should be made for the careful bacteriological examination of all suspected cases.

III.

Fever in various forms has proved more destructive to armies in the field than powder and shot. It has been well said that bullets and bacilli are as Saul and David, "Saul has slain his thousands and David

his ten thousands." The story of the destructive character of fevers has never been so well demonstrated as in the great Civil War of the United States, during which malaria, dysentery, typhoid fever, and other diarrhoeal diseases were fatal foes. Woodward's *Report of the Medical History of the War of the Rebellion* is a perfect storehouse of information on camp diseases. It is not easy to pick out the exact percentage of typhoid fever, as a large proportion diagnosed as diarrhoea and many of malaria belong to this disease; but the official figures for the army of the North are sufficiently appalling—79,455 cases and 29,336 deaths! There is the same story in the Franco-Prussian war; among the German troops there were 8,000 deaths from typhoid fever, 60 per cent. of the total mortality! It is said that the typhoid fever existed in every army corps at the outbreak of the war, and the campaigns were carried on largely in infected regions. I have already referred to the terrible experience in the Spanish-American war among the volunteer troops in the home camps. The sad memories of the South African war still haunt the memory. That was a war which brought out many new details in campaigning, but the sternest lesson taught is the one we are now considering, as it, too, was a war in which the bacilli counted for more than the men. Of the 22,000 lives lost, the enemy is debited with only 8,000; preventable febrile diseases for 14,000. And amongst these, as usual, typhoid fever headed the list, 57,684 cases, of whom 19,454 were invalided, and 8,022 died. The *Bacillus typhosus* alone did more damage than the Boers. Here again, as in the Spanish-American war, it was not so much water-borne typhoid as camp infection by fingers, flies, dust and food.

We are now in the fourth month of the war, and, so far as one can gather from the somewhat meagre reports, the health of the troops at the front has not been damaged to any extent by fever, and, so far, the sad losses have been from bayonets and bullets. On active service the soldier may take typhoid fever with him, or he may find it in the country. A large body of men has a certain percentage of carriers, any one of whom may act as a focus of distribution. The conditions in camp life are peculiarly favourable to case infection; thus it would be impossible for a carrier cook not to contaminate the food of an entire company. Of equal moment is the state of the country in which the troops are working. During the Spanish-American war it was

not possible in the United States to locate a camp in a typhoid-free position. In this country it is not possible to pitch a camp in an infected district. In South Africa both conditions prevailed ; infection was brought by the soldiers, and was abundant in the country. It seems not unlikely that the troops in France and Belgium are reaping the benefit of the past ten years of active campaign against typhoid fever. Details are not at hand as to the prevalence of the disease in the eastern and north-eastern regions of France, but I am told there has been a great reduction in the incidence of the disease in Belgium, and that the troops have heretofore suffered but little. The Rhenish provinces should reap the benefit of the remarkable antityphoid campaign of the past ten years. Certainly it is very gratifying, particularly at this season of the year, that comparatively few cases have occurred. Among 2,000 German, English and Belgian troops who have been, or are at present, in the base hospital at Oxford, there have only been five cases of typhoid fever ; and this, I believe, to be the experience in other large hospitals throughout the country. It will be a great triumph to go through this war without a devastating experience of typhoid fever. In the fighting line it is not possible always to ask the soldier to carry out sanitary precautions, and in a very infected country, even with the best of intentions, he cannot avoid exposure. Here we may expect to find the protective value of inoculation, and it is very satisfactory that the value of the measure has been so generally recognised by officers and men. An immense proportion of those who go with the Expeditionary Forces will have been protected—for a period at least. While with our present knowledge we cannot but regret that the inoculation has not been made compulsory, let us hope that a sufficient number have taken advantage of the procedure to make impossible a repetition of the enteric catastrophe in South Africa.

In the midst of this great struggle we stand aghast at the carnage—at the sacrifice of so many lives in their prime—

That many men so beautiful,
And they all dead did lie.

The bitterness of it comes home every morning as we read in the Roll of Honour the names of the much loved sons of dear friends. Strange that man who dominates Nature has so departed from Nature as to be the only animal to wage relentless war on his own species.

But there are wars and wars, and let our thought to-night be of the other army waging peaceful battles against our true foes. No one has so well contrasted the work of these two armies as the poet laureate of the profession, Oliver Wendell Holmes—

As Life's unending column pours,
Two marshalled hosts are seen—
Two armies on the trampled shores
That Death flows black between.
One marches to the drum-beat's roll,
The wide-mouth clarion's bray,
And bears upon a crimson scroll,
"Our glory is to slay."
One moves in silence by the stream,
With sad yet watchful eyes,
Calm as the patient planet's gleam
That walks the clouded skies.
Along its front no sabres shine,
No blood-red pennons wave;
Its banner bears the single line,
"Our duty is to save."

We shudder at the needless slaughter of the brave young fellows— allies and foes alike—but think of the slaughter which goes on in our homes, just as cruel as, often more cruel than, that of the battlefield! Tuberculosis alone will kill more than ten times as many this year in Great Britain than will die abroad for their country. Comparing the death-rate in England to-day with that of fifty years ago we may say that, as a result of the work of the other army, more will be saved from death by enteric fever in 1914 than will be killed this year in the war. Eberth's *Bacillus typhosus* will kill in 1914 in the United States more than will German shrapnel and bullets in the Expeditionary Force. Moving in silence, the great army of sanitation, with a general staff and leaders of all lands and languages, claims allegiance only to Humanity. In war it has not often fought winning campaigns, but the new knowledge is full of such promise that even the vanquished may be victors.

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The PRESIDENT: Ladies and Gentlemen, I think your acclamation sufficiently conveys to Sir WILLIAM OSLER the great pleasure we have all had from his discourse. We naturally expected something poetic, and we have had it, because he began with Homer and ended with Holmes.

Before calling upon Sir JOHN BROADBENT to open the discussion, I should just like to draw attention to the idea of a possible relationship between enteric fever and tuberculosis. Many of us are aware that LOUIS and COMBE, of Paris, shewed experimentally that antityphoid vaccine brings out latent tuberculosis in cases where it is present. I should like to have Sir WILLIAM OSLER's opinion on that.

I think his statement regarding inoculation was exceedingly fair, and detailed all the minor troubles incidental to that small operation.

Regarding India, I may mention that ten years ago the admission rate for enteric fever per thousand men was 19·7. The admission rate now is less than 2·6 per thousand. Ten years ago the death-rate from enteric was over 3·7 per thousand. The death-rate at present is ·39 per thousand, taking the whole Army. At present, amongst the inoculated in India, the case mortality is only 12·8 per cent., whilst amongst the non-inoculated it is 40 per cent. These are fair numbers, and prove the necessity for inoculation.

Sir WILLIAM OSLER drew attention as to what should be done with convalescents. If this country could take a lesson from India we should be following a good example. In India there have been established enteric fever depots—Naini Tal and Wellington. What are these used for? To them are sent convalescents from enteric and paratyphoid, also cases of pyrexia of uncertain origin, together with all proved chronic carriers.

Shewing the necessity of internment of cases of pyrexia of uncertain origin is the fact, that of 138 cases sent to one of these depots, five were excreting paratyphoid A bacilli in the fæces. I would ask Sir WILLIAM OSLER, in his reply, to refer to the possible relationship, or danger, of inoculation against enteric fever in cases of latent tuberculosis.

Sir JOHN BROADBENT: When I came here this evening I had no intention of speaking or of opening the discussion. This is a subject in which I am very greatly interested, and I was extremely interested in hearing Sir WILLIAM OSLER's paper. I was very surprised the other

day, in passing a certain antivaccination shop in the neighbourhood of Covent Garden, to see Sir WILLIAM OSLER's name in large letters in the window. I wondered what Sir WILLIAM OSLER had to do with anti-vaccination, and found that it stated Sir WILLIAM OSLER was enquiring for any untoward results of antityphoid inoculation. It set out a long list of the horrible things which they stated might occur, and Sir WILLIAM OSLER's name was being used as an argument against antityphoid inoculation. I think, if he is passing that way, he should take some steps to suppress that notice.

There are one or two points I might mention. Sir WILLIAM did not touch upon paratyphoid. It so happens that this year I came across three cases in St. Mary's Hospital of paratyphoid, and I take it that the antityphoid inoculation will not be protective against that. It was curious that these three cases were not connected with each other. I think paratyphoid is a much more insidious disease than typhoid—the patient is not so ill, abdominal symptoms are not prominent, and it is seldom fatal. It is possible that this class of case may often go undetected unless carefully investigated.

I think the point about carriers is very important, and they are often very difficult to detect. There was a case at the Naval Hospital at Chatham, which I saw recently, of a man who had been a carrier for eight or ten years, and had started an epidemic of typhoid in every ship on which he had been. They had him there perfectly well, and he strongly resented being detained. It is difficult to know what to do with this type of case. Every kind of treatment has been tried—inoculation, intestinal disinfectants of every kind have been tried, and none of these efforts seem to be successful. I doubt if we could do as they do in America, and intern these people for an indefinite period. It is one of the most serious problems we have to face, how to get rid of the organisms in these cases; and I think, if one looks back on many sporadic cases, one could perhaps justifiably attribute them to carriers.

Another point which, I think, is of considerable importance, and which Sir WILLIAM OSLER did not touch upon, is the question of the disposal of the sewage in camps. In many of these camps the system is very primitive. There are pails of water into which the men defæcate, and it is carried off in a cart. I do not know what becomes of it eventually. I was interested the other day meeting two gentlemen,

inventors of the process, and hearing of the S.O.S. system now carried out at Aldershot and Wimbledon. By this system the whole of the sewage is treated with superheated steam and certain chemicals, of which I do not know the details. As a result of this treatment valuable by-products are derived: a certain amount of oil and fat, light oils suitable for internal combustion engines, and a large proportion of sulphates. It is claimed that sewage can be treated by this system and a profit of ten shillings per ton made, the residue, apart from these chemical products, being simply dried carbon. Another means of treating the sewage is by taking the stools, mixing them with sawdust, and burning in a destructor. This is, of course, a very effective method, and not particularly costly. It seems to me that this difficulty in camps of dealing with a large quantity of wet sewage must become a very serious problem, especially in wet weather, when the soil gets thoroughly permeated and sewage farms will not absorb it. Happily, so far, we have not heard of any cases of typhoid in these camps, but it is a very serious problem planting camps in country villages, with a vast amount of sewage, and no really safe means of dealing with it in case of an epidemic. As to what happens to the sewage in the trenches, I should be afraid to speculate; and it would be very interesting to hear from those who have been out at the war how they attempt to deal with it, especially when the trenches are flooded, and there is no possibility of the soil soaking up the excreta. The disposal of sewage is an important problem at the present time, in view of the number of men who are scattered all over the country in camps.

Dr. WALTER BROADBENT: Sir WILLIAM OSLER has asked me to take part in this discussion, as I have seen six cases of illness occurring after inoculation in men who have been sent in to the Brighton Territorial Hospital from the camps in Sussex.

The first of these had been inoculated for the first time on October 6th. He felt seedy, but did not go to bed. The next day he had a rigor, and was admitted to the field hospital with a temperature of 104. The following day he was sent in to Brighton. He then had pneumonia of the right middle and lower lobes, and of the left lower lobe. His pulse was 130. His tongue was dry and brown; his teeth very decayed and surrounded by foul pyorrhœa. He was very delirious, and never

responded to treatment, dying on the seventh day after admission. After inoculation the men are given 36 hours off duty, but are not sent to bed. Probably in this case the man was loafing about the camp with a raised temperature, and contracted a chill, which gave him the pneumonia.

My next four cases were all of one type, varying in severity. They had all been inoculated for the second time and had not felt particularly ill. Six to eight days later each reported sick complaining of headache, and was then found to have a raised temperature. They all had large very furred tongues. Their bowels were constipated. The temperature in the most severe case was 103·4 on the first day, 102·2 on the second, 102 on the third, and had fallen to normal by the eighth day. In the other cases the temperatures were not so high, and lasted three to seven days. There was no other complaint than of headache. Three of these men were inoculated on the same day, and the fourth a day later, all in the same camp; so it looks as if there might have been something wrong with that lot of vaccine, but a large number of other men were inoculated at the same time with no after trouble. These men were all fit for service within three weeks. The interesting point about them was the incubation period of six to eight days, during which they felt all right after the inoculation.

The sixth case was only admitted on the last day of my month on duty, and is at present under the care of Major HALL. This man had been inoculated for the second time two days before. He had a temperature of 103, was very delirious, and complained of intense headache. This was so severe that a lumbar puncture was done on the fourth day, but there was nothing abnormal in the cerebro-spinal fluid, and no increased pressure. An urticarial, almost purpurial, rash developed on the exterior surfaces of the arms and legs, which lasted a few days. His temperature varied between 100 and 102 for the first fortnight, and the headache and delirium persisted. The tongue has been very furred and the bowels constipated all the way through. In the last five days the temperature has not been so consistently high, and there is only delirium when it is up, but he has had three rigors. He still has headache, but not so severe. Nothing has been found to account for the rigors, and he appears to be much better than a week ago.

I do not know if the treatment of enteric comes within the scope of this discussion, but I should like to recommend the use of an ice bag. I should suspend it from a cradle over the right side of the abdomen in the region of the lower part of the ilium. It is important that there should be nothing between the ice bag and the skin but a piece of gauze or butter muslin, so that the cold may penetrate as far as possible.

Medicinally, I think there is nothing to equal Sir WILLIAM BROADBENT's prescription of quinine sulphate gr. 2, dilut sulphuric acid $\text{m}5$, liquor hydrarg. perchlor. $\frac{1}{2}$ drachm, every four hours—not within half an hour of food. If the diarrhoea is excessive, the sulphuric acid can be increased, and if there is constipation, magnesium sulphate can be added in sufficient quantity to produce one or two actions of the bowels a day. The use of the sulphuric acid and magnesium sulphate also have a tendency to diminish the risk of hæmorrhage. As an illustration of the efficacy of the ice bag, combined with this medicine, I might quote a case occurring in a slightly wounded soldier, who was transferred to my ward on the second day. The temperature which had been 103·8 the day before, was 104·5 when this treatment was commenced. In 24 hours it fell to 101, and only once afterwards rose to 102. He had had diarrhoea for four days before admission. There was very marked tenderness in the right iliac region and enlargement of the spleen, which was also tender. 2ViWidal reaction was negative at first, but strongly positive at the end of a week. He had never been inoculated. It was a case in which one would expect deep ulceration and possibly hæmorrhage, but he has done exceedingly well, never giving rise to any anxiety.

Dr. F. W. GOODALL: I am very glad Sir WILLIAM OSLER has so firmly insisted upon the value of antityphoid inoculation as a preventive of typhoid. I think the figures to which he has alluded are practically conclusive of that, so far as figures can be, and those relating to our Army in India have passed the tests of the finer mathematical methods introduced by Professor KARL PEARSON some years ago. I think the figures of the American Army are the most convincing of all. I believe I am right when I say that the American Army is practically the only one where compulsory inoculation is enforced.

I was rather disappointed that Sir WILLIAM OSLER has not been able to obtain some information as to the prevalence or absence of typhoid amongst the troops engaged at the Front. Apparently he has been kept as much in the dark on these matters as the general community. One knows from official statistics that just before war broke out there was typhoid in Paris and in some of the Belgian towns. There are in my hospital at present some six patients from amongst the refugees from Belgium, so that there is no question of there being typhoid in the region of the War. I have read a large number of the reports in the papers and I have noticed allusions to enteric fever only in two. One was in *The Times* last Saturday, in which the Special Medical Correspondent boldly stated they had solved the problem of the carrier cases. The other was in the *Guy's Hospital Gazette*, whose Paris correspondent wrote of enteric wards. I had hoped for more information on this subject,

As to the reaction set up by inoculation, I have had very little experience of inoculating healthy people. I have tried inoculations in a considerable number of cases of the fever itself for purposes of treatment, and I am on the whole disappointed with the results. In two cases, however, I did see some very remarkable results, which I think were due to the vaccine. Before I mention these cases, I may say that nearly every case I have inoculated has had no reaction at all. This fact has surprised me. I should have expected all the cases to have got a reaction, but, with two exceptions, there have been no reactions. Both these cases had, a few minutes after inoculation, a rapid rise of temperature and a rigor, and in both cases the temperature came down to normal after the rigor and stayed there, though previously the temperature had been continuously raised. I think in these two cases this result was due to the vaccine. I have seen nothing like it in other cases.

I was glad to hear that Sir WILLIAM OSLER had investigated the story of the alleged untoward results at Aldershot, because it has been widely circulated in the medical world, and it is well that its falsity should be publicly demonstrated. It will be very interesting to see if the antityphoid campaign which the Germans have been carrying on for so many years in the Rhine provinces, will have any effect on the prevalence of typhoid amongst the troops; but if the latter are

protected by inoculation, it will be difficult to decide whether the absence of typhoid (if it be absent) is due to the inoculation or to the sanitary measures.

Paratyphoid fever has been alluded to by Sir JOHN BROADBENT. From my experience I should say that it is impossible to distinguish between paratyphoid and typhoid on the symptoms alone; bacteriological examinations are necessary.

On the question of carriers. I am very sceptical as to the importance of the carrier. I do not know whether Sir WILLIAM OSLER has read the presidential address of Dr. THEODORE THOMSON, of the Local Government Board, which was delivered before the Epidemiological section of the Royal Society of Medicine some four years ago. In that address a large body of evidence was brought forward to shew that the importance of the carrier was much exaggerated, so far as this country was concerned. Dr. THOMSON put the number of carriers in this country at from 100,000 to 110,000, and yet the disease is getting progressively less and less. He shewed that after the epidemics in Maidstone, Worthing and Lincoln, in which towns there must have been a large number of carriers for some years after the epidemics, the incidence of typhoid was considerably less than it had been in the years before the epidemics; from which he concluded that typhoid carriers have not very much influence on the general prevalence of the disease. In the camps in the Southern States of America, during the Spanish American War, it was not a question of carriers, but of persons actually suffering from typhoid in the early stages. They had diarrhoea, and want of care led to the infection of the ground, blankets and so forth, and so the disease spread. Fortunately, this is not taking place in our camps now, because this is not a typhoid country, and precautions are being taken. American hamlets and towns are now much in the same state as regards sanitation as we were here, in this country, fifty or sixty years ago. I will bring my remarks to a conclusion by stating that if, as we believe, inoculation is of value, it does not matter a rap if typhoid is introduced amongst our troops, nor by what means it may be spread, so long as all, or nearly all, the men are protected by inoculation.

Dr. NEWTON PITT: A man under my charge was inoculated against typhoid on September 29th. Three days later he developed pain in his ankles, knees, and elbows, with great pain in his eyes from a fairly acute sclerotitis; this was well marked on admission on October 6th. The temperature did not fall till the 11th, when the arthritis had subsided and the sclerotics had cleared up. He has had two relapses of sclerotitis and arthritis since, with pyrexia. The condition is similar to that often associated with gonorrhœa. There was no gonorrhœa, pyorrhœa, or other septic centre to be discovered. I am putting the case on record, as I am not aware that a similar sequel has been noted.

Fleet-Surgeon P. W. BASSETT-SMITH: There is no doubt that one hears much more to-day with regard to the Army. I would like to say that the campaign is being carried on just as strongly in the Naval Services for those employed on shore. Practically every officer is inoculated when he enters the Navy. It is not compulsory, but very little objection is raised. The large concentration camps report that inoculations are being carried out extensively.

The reason I rose was that Sir WILLIAM OSLER asked for untoward results. I heard this morning of a case, and it falls into line with one noted just now. A man was inoculated first, and on the eighth day he had the second inoculation. Two days afterwards he was notified as suffering from enteric. This man had definite symptoms of enteric, and the question is, is it a case of rapid incubation, or is it a case of inoculation after infection from outside, or what is the true reason for it? It is one of these cases which is sure to be very much talked about. It is sure to influence very much the men in the camps, and we must recognise that sometimes these unfortunate results do occur. It may or may not have anything to do with anti-typhoid inoculation.

With regard to the question of carriers. I was on one of the big battleships where case after case occurred. We tried hard to find the cause, and by going through a large number of the men and examining their stools, we found the carrier, and after that it was definitely established that it was this man. His history was traced from ship to ship, and wherever he had been typhoid had broken out.

So that it is important in the Navy, as in the Army, to localise and get rid of the carriers.

Dr. J. M. ATKINSON: The remarks I have to make are more in the nature of enquiries. May not the malaise induced by the anti-typhoid inoculation so diminish the normal physiological resistance to infection, that the question arises whether it is wise to inoculate troops immediately before going on active service? I have had two cases within the last three weeks. One of them is a nephew of mine, in the London Scottish, and within three days of the first inoculation he developed a typical attack of influenza. The other case was a lieutenant in the Queen's Westminsters, who within eight days of the second inoculation developed acute Bright's disease, the cause of which was exposure to wet and cold. These are two cases in the practice of one doctor. With reference to a previous attack of typhoid fever, I would ask whether it is necessary for a soldier who has once had typhoid fever to be inoculated. I have a relative in the Sportsmen's Battalion. He had an attack of typhoid fever when he was fifteen years of age, and there is a question as to whether he ought to be inoculated. How long does one attack protect an individual from a second attack of the disease?

Dr. BASIL PRICE: I desire to ask Sir WILLIAM OSLER some questions concerning vaccines. There were some interesting papers read at the Far Eastern Congress two years ago on the question of the use of living attenuated germs in connection with plague. Much better protection was obtained when living attenuated cultures were used than when ordinary vaccines. Does Sir WILLIAM OSLER know of any results from the use of living attenuated cultures of typhoid germs or the effects following their use? Secondly, are any vaccines in use containing more than one type of germ, paratyphoid and typhoid? Many of us are interested in this question, and also another, namely, whether local strains or those from India or China could not be better used than those we have at home, for people proceeding to those parts?

Dr. F. M. SANDWICH: I should like to say one or two practical things about inoculation, with which I hope the reader of the paper will

be in sympathy. I suppose we shall all allow now that at least two inoculations are necessary. In the South African War the question was not settled, and many people had one injection and were not saved, when two injections would perhaps have saved them. Then the site of the inoculation. I believe it is common now that inoculation should be done in the outer arm, the seat of the deltoid insertion. It is not a very good site, I think, and I have suggested this to Army medical officers. It is obviously a part of the body which is easily exposed to injury. It would be much better if it were done three inches under the clavicle. There is also the question about reaction after the second injection, for many doctors are under the impression—gathering from what I am told by patients—that there may be a reaction after the first injection, but not after the second. That is not always so. Many people suffer more after the second injection than after the first. A more important point than any I have mentioned, is the necessary and compulsory rest after each inoculation. Some of the speakers have told us of untoward results. I have not seen any, after about a thousand injections. They mention that the men are usually walking about. I have had the opportunity of discussing this question in hospital with several privates and non-commissioned officers belonging to different regular regiments, and they told me that after their inoculations they were told they could lie about, and in the afternoon, Sunday—a day of rest presumably—were told that anybody who wished could come out for a route march. Five or six in each regiment came back in a fainting condition. Now, I suggest that that is not the way to treat the inoculation of an important vaccine. The men should be compelled to have twenty-four or thirty-six hours' rest; whether it is actually necessary to put them to bed I do not know. At any rate, they should not march.

I was glad Sir WILLIAM OSLER mentioned the segregation of typhoid cases. Some day in our general hospitals in London we shall learn that and recognise there is some risk, especially to nurses, in mixing up our typhoid cases. In the South African War we divided our hospitals into three sections: medical cases not typhoid, surgical cases, and typhoid cases. We assumed one-third would suffer from typhoid—they did; and in spite of that care, some of the nurses and orderlies contracted typhoid in the typhoid section until we took to having an incinerator, which is the best method of dealing with excreta.

The question of the carrier is, of course, of great importance in places like India, and the instances you have mentioned of the camps for typhoid carriers are extremely interesting. I heard a few days ago of a medical officer from the neighbourhood of Bristol. He had a typhoid carrier and did not know what to do with him. In England the custom is when you are tired of your typhoid carrier you send him home, and trust that Providence will take care of him. This man was warned not to enter any trade likely to interfere with the health of the community. The medical officer, having perhaps some qualms of conscience, traced him, and the first place he found him in he was ladling out milk in a dairy. He took the trouble to call on the owner of the dairy, and pointed out he would lose all his customers, either from fear or from typhoid. He was dismissed from that and was then heard of in a bakery establishment. He was dismissed again, and then he was found a job, appropriately enough, in a cemetery.

Dr. R. A. O'BRIEN: Some time ago I came across, in an American paper, an exceedingly ingenious way of dealing with typhoid stools. Disinfection of typhoid excreta whether in small or large quantities is very difficult. If one does add disinfection to fæces, one needs some means of bringing the disinfectant into contact with the individual bacilli, and one can imagine a squad of men turning with forks the mass of fæces in the trenches in order to mix the disinfectant thoroughly with the fæces. This person used lime, not as hitherto used, but simply as a means of giving heat. I have lost the reference; probably Sir WILLIAM OSLER will know it. The method consisted in adding unslaked lime to a cup of hot or boiling water, and the mass was poured on the single stool. Without any mixing, the heat generated was sufficient to kill all the bacilli in the stool. If that method has been confirmed, it is one of the most valuable I have come across.

As regards typhoid at the Front. One item of news has reached me that a serious outbreak has occurred at Roubaix and Lille, brought by the German troops. If it is so, it would be an ironical commentary on the lack of recognition in the German literature of the valuable, practical work carried out in the British Army, demonstrating the value of protective typhoid vaccination.

Sir WILLIAM OSLER: I am very sceptical about the close relation of tuberculosis and typhoid, though I know our French brethren regard it as a not infrequent sequel. I do not think that among the 1,500 cases at the Johns Hopkins Hospital tuberculosis directly followed in a single instance. I have made the mistake in diagnosing an acute case of tuberculosis as typhoid, and I have a typhoid-like toxemia in a comparatively small lesion in tuberculosis. I do not think that the records shew that inoculation for protective purposes has been followed by tuberculosis. Did you say there had been cases reported?

The PRESIDENT: Experimental cases.

Sir WILLIAM OSLER: With reference to what Sir JOHN BROADBENT saw in the anti-vaccination shop, it is a great deal better to pull these fellows into the open, and meet them there. The public ought to know everything necessary. If you attempt to hide anything it is only magnified. To know that occasionally after antityphoid vaccination severe symptoms occur need not alarm them. The important matter is to be honest and deserve the confidence of the public.

Clinically there is not much to choose between paratyphoid and typhoid. The germs are half-sisters and behave just the same way, and the cases often can only be distinguished bacteriologically,

The question of the disposal of the sewage is important. It is satisfactory to hear that the Medical Officers of Health throughout the country have the matter in hand.

I am indebted to Dr. WALTER BROADBENT for reporting his interesting cases.

Dr. GOODALL spoke with reference to typhoid at the front. We really have not got full information. My information is all indirect, obtained from the wounded at the hospitals I have visited. There have been very few cases of typhoid returned to this country, and so far as I can gather there is very little at the Front, so far.

I did not like to hear what Dr. GOODALL said about the carrier. Would anyone like to have a carrier cook in his house? It is a question of occupation largely, and there is not much risk, if, in the calling, there is not much chance of contamination. The main thing is not to have the typhoid. We shall not be able to say of the Rhenish

provinces, which we may hope to occupy in a short time, whether the absence of typhoid (as we hope will be the case) is due to inoculation or whether to the fact that it is not there.

I agree with Dr. SANDWITH that the site usually chosen for inoculation is not a very comfortable one. Every movement of the man's arm affects it. I agree, too, with what he says about segregation, except in one particular—the general hospitals connected with the medical school. I have always maintained that a student should know two acute diseases well—typhoid and pneumonia. With typhoid fever out of the general wards, it is a very difficult thing to give students a proper knowledge of the disease. Moreover it is a test for students and nurses. An outbreak of typhoid fever means the wards have not been conducted properly.

I am glad to hear from Fleet-Surgeon BASSETT-SMITH that the Navy are carrying out the inoculations so thoroughly. Dr. ATKINSON raised the question of lowered resistance after inoculation. This is one reason why care should be taken to give the men a day or two off, and they should not be sent off at once after their last inoculation.

A CORRECTION.

In the last number of the TRANSACTIONS of the Society of Tropical Medicine and Hygiene, for November, 1914, on page 25, line 19 "BRODEN, 1914," should be "BROPEN, 1904." It is important to note this date, which refers to the name *Trypanosoma congolense*.

TRANSACTIONS OF THE SOCIETY OF TROPICAL MEDICINE AND HYGIENE.

JANUARY, 1915.

VOLUME VIII. No. 3.

Proceedings of a Meeting of the Society on Friday, December 18th, 1914,

Dr. F. M. SANDWITH, F.R.C.P., *Vice-President*, in the Chair.

TROPICAL PROBLEMS IN THE NEW WORLD.

BY

ANDREW BALFOUR, C.M.G., M.D.

To anyone gifted with what we may call the "sanitary eye" the most interesting notice on board a Royal Mail steamer bound for West Indian and South American ports, is one which is to be observed in the closet compartments, and which is printed in Spanish and in English.

"Please do not throw paper on the floor," is the injunction. To the uninitiated this suggests a laudable desire for tidiness. Its real significance is not apparent until one embarks upon a South American river steamer, or penetrates into Venezuela or Colombia; but of this anon.

We will begin with Barbados, a tight and loyal little island, the outpost of our Empire in the West. There is nothing very tropical about Barbados, when viewed from a steamer in the roads. Save for a fringe of Casuarina trees, resembling Parkinsonias, and an occasional palm, one might be gazing at a bit of southern England transported to the Caribbean Sea; but as soon as one nears the shore this illusion is dispelled, for the coral formation is apparent, together with other features inseparable from hot climates. Still employing the "sanitary eye"—a very useful asset in such journeyings, and one as a rule more agreeable

to use than the "sanitary nose"—we observe the large number of small craft, mostly schooners, tied up alongside the wharves, and lying in the carenage. We enquire whence they come, and we are told that they hail from the neighbouring islands, British Guiana, and the Orinoco. At once we are confronted by an interesting problem. Locally acquired malaria is unknown in Barbados, for the simple reason that anophelines are not present in the island. Why are they not in evidence? Granting for the moment that there are no suitable breeding places for them, or that natural enemies abound and prevent them propagating themselves, how comes it that they are not introduced by these small craft, hailing from regions where they are common and very often infected with the malarial parasite?

It is true that the anopheline is not nearly so good a traveller or seafarer as the hardy stegomyia, but still we know that he, or rather she, can be carried long distances on steamers, as, for example, from Bombay to Trieste, and occasionally from the Southern Nile to the desert areas of the Sudan.

I questioned Dr. BRIDGER, the able and energetic Port Health Officer of Bridgetown, on this matter. He told me that he had searched the vessels for them, but had never been successful in finding them. In a letter which he sent me some time ago, he says:—

"I have myself often wondered that mosquitoes do not find their way here on these craft; but have never yet discovered one, though I have looked for them both before and since you referred to the matter. We have about half-a-dozen white men—natives of Saba—who are masters, and usually owners, of these craft, and I have discussed with them this question. They tell me that lying alongside the wharves in British Guiana (Georgetown), mosquitoes come on board in large numbers—probably many anophelines among them, for malaria is quite common there—but on getting to sea they disappear entirely, as a result, in their opinion, of the strong breeze blowing them away. Barbados is to windward of all the neighbouring malarious ports, and therefore sailing vessels have to "beat," as it is called. Making these several tacks they would get swept by the wind first on one side and then on the other.

It is conceivable that every mosquito on deck or in the living

compartments, which are only deck houses, could be swept away, as they are very fragile. As to those which may be concealed in the hold, we must conclude that the tight battening of the hatches, for not less than thirty-six hours, must be sufficient to kill them."

It may be so, it probably is so, but I would like to see a few ideal breeding places artificially constructed in close proximity to the wharves. It would be very interesting to observe what such a kind of trapping produced. I suggested this manœuvre, but was told that it would immediately result in a campaign of calumny, and that any hapless medical man who tried it would run the risk of being accused of enticing deadly insects to the island!

Barbados is justly proud of a fine conservatism, but it may be and is carried too far in sanitary matters.

Let us go a step further in our malarial enquiries, and at the same time a step back. The first will bring us to a consideration of possible anopheline breeding places in Barbados, the latter will refer us to the statements made by Dr. MALCOM WATSON in this very room a twelve-month ago, and the remarks of Dr. LOW thereupon. Dr. WATSON declared that the absence of breeding places was due to the porosity of the coral limestone of which Barbados is composed. Dr. LOW stated that such a conclusion was not justifiable, and cited the presence of permanent water collections near Worthing. That Dr. LOW was correct is apparent from the photographs I was able to take, shewing the extensive Hastings swamp with its accompanying canals, and also certain pools which look ideal for anopheline breeding operations, a photo of which is given here (*Plate 1, fig. 1*). On at least one estate there is also a large pond which might very well play the part of a mosquito nursery. Both Drs. WATSON and LOW agreed that the presence of the famous Barbados "millions" cannot be the sole cause of the absence of eggs, larvæ and pupæ, and Dr. LOW has shewn that, so far as the Hastings swamp is concerned, there is nothing in the chemical constitution of the water adverse to mosquito life. I brought some of the "millions" home, and had them named at the British Museum. They are not *Girardinus pæcilloides*, but *Lebistes reticulatus*, a point worth noting. I shew you some specimens.

Are there any other enemies which may play a part? In the pond

aforesaid there were ducks, and these might certainly be effective, while the swamp is actually maintained as a shooting ground. It attracts flocks of migrating birds, and these would probably play havoc with mosquito larvæ, but only at certain times of the year. In my search I came across another enemy, very abundant and very voracious, which seems to have been overlooked. This is the little back-swimmer, belonging to the genus *Notonecta*, which, by means of its active movements and its silvery belly, is easily recognised. It might well be named an aquaplane, for when speeding through the water it closely resembles an aeroplane upon the wing. WILLCOCKS, of Cairo, was the first to draw attention to the larvivorous habits of these useful insects. I tested them at Khartoum and was interested in coming across them again. The indefatigable Dr. HUTSON being with me, I pointed them out to him, and he told me that he had been puzzled by one water collection which contained no "millions," only these *Notonectidæ*, and though in every other respect suitable for culex or stegomyia larvæ, was quite mosquito free. He had suspected the back-swimmers, but was told they were inoperative. We soon found the contrary, and spent a profitable Sunday afternoon watching them fasten on culex and stegomyia larvæ, which they grip as a spaniel grips a rabbit, and then engulf, tail first. When you convey these back-swimmers from their native haunts in a vessel or jar you have to be careful that the latter is covered, for these curious creatures have a habit of reaching the surface, rapidly drying their wings, and flying forth. As I was journeying in the mule train from Hastings to Bridgetown, one of my specimens played me this trick. It is known that these *Notonectidæ* sally forth from their pools at night and seek fresh hunting grounds.

Now I am far from saying that the recognition of larvivorous *Notonectidæ* in Barbados solves the mosquito problem there, but they may certainly play a part in keeping pools and swampy areas free from larvæ. It would be well worth someone's time to investigate the question thoroughly.

Dr. SAMBON tells me that in the rugged northern part, known as Scotland, where, at certain seasons of the year, there are running streams, the presence of natural oil may be the reason for the absence not only of the water stages of the mosquito, but of all aquatic life in these temporary rivulets. I am unable to express an opinion on this

view, as I only gazed upon St. Andrew's parish from one of the highest elevations in the island. I got there through the kindness of Dr. HUTSON, who has done so much for the island from a sanitary standpoint, and who pursues the wily *stegomyia* with an ardour which deserves success. Is it not, however, a disgrace that in a little island like Barbados, where there are few natural breeding places, *stegomyia* and *culex* still flourish exceedingly? Given full powers and adequate assistance, more especially in the direction of trained British Sanitary Inspectors of the right type, I believe that Dr. HUTSON, or any other energetic and tactful Health Officer, could clear Barbados of harmful mosquitoes within a year; that is to say, he could reduce them in numbers till they were no longer a potential or actual source of danger to the community.

On the contrary, what do we find? Despite the great advantages accruing from a pipe-borne water supply, despite Dr. Low's and Professor BOYCE's campaigns, despite tales of comparatively recent local outbreaks such as that in 1908, despite the presence of the well-known Yellow Fever House, despite Dr. HUTSON's work, *stegomyia* are still busy breeding in barrels, tanks and other convenient places provided by the negro smallholder, and too often also by the European. The inhabitants, if ever they think about the matter at all, rely on their Port Health Officer. They might do worse, but they might certainly do a great deal better, and meanwhile are contented to be pestered and bitten by a voracious blood-sucker.

Conditions are even worse when we consider the *culex* mosquitoes. These abound in some parts and, sad to say, filariasis is far from uncommon, and so elephantiasis is to the fore. Indeed, Barbados is acquiring an evil reputation, and the phrase "Barbados leg" is coming into use. Is it fair or right that young and otherwise healthy people should be afflicted with an easily preventable disease like elephantiasis? Is there any rhyme or reason for tolerating a state of things where possibly, through no fault of their owners, a man's scrotum may eventually reach his knees, or a woman's graceful leg and foot attain huge and hideous proportions? In some countries the difficulties of getting rid of the mosquito carrier of *filaria* are well-nigh insuperable, but this is not the case in Barbados, and it is amazing at this time of day to see the lethargy and indifference with

which the mosquito question is treated; and it is both amazing and disheartening to be told of the opposition which Dr. HUTSON's diligent efforts encounter.

There is only one way of dealing with this kind of thing, and that is what we may call the punitive method. Offenders must be fined—tactfully fined, but well fined—until they learn that it is better to keep an eye on their water receptacles than to be frequently called upon to pay a penalty. The system is in force in Barbados, but organisation is lacking. Full powers must be accorded the Health Officer, who should be well paid and devote all his time to sanitary work. He must be given a sufficient and efficient staff. It is absurd that a man of Dr. HUTSON's years and standing should have to go wandering about amongst negro cabins, dipping cups and calabashes into barrels, and wearing himself out in duties which could be performed by a young and trained assistant, thus setting free his chief for grappling with some of the other problems which Barbados presents.

There are many such. I might speak of the "Poor Whites" of whom we heard when our PRESIDENT delivered his inaugural address, but I will keep them until we get to Grenada. The guinea-fowl in Africa is a pathological museum. The blood of those I examined in Barbados shewed no hæmatozoa. Neither did the blood of some captive migratory birds, but, for all that, an interesting piece of work would be to determine the blood parasites of the wild and domesticated creatures of the island. It has never been done, but it should be done, and I think Dr. JOHNSON, Director of the Laboratory, is the man to do it. He is keen and has a very fair equipment, but he needs assistance and a larger annual contingent. At present he has too much other work to do. Still, there is hope in that direction.

The Barbadian leper would form an interesting subject of study. Why did pigs, which were once kept at the leper asylum, develop a curious disease, associated with skin lesions, when fed, *horribile dictu*, on the old poultices and dressings? This economical practice is no longer in force, but it appears that an opportunity for research was lost. At the same time, the rats there are affected with what may be rat leprosy, so a part of the field is still open to the anxious enquirer! Why does pellagra flourish when there are no *Simuliidæ*?

Do *Ceratopogoninae* play a part, or are insects operative at all? What is the best way of dealing with crab holes, the breeding places of *Deinocerites*?

However, I must not let Barbados detain us any longer, so we will away to a very different type of island, a veritable pearl of the Antilles, the green and picturesque Grenada. But though Grenada differs in many respects from Barbados, I regret to say that they have at least one thing in common, and that is the prevalence of *Aedes calopus*, as *Stegomyia fasciata* has been renamed by KNAB. St. George's is full of this annoying insect, and again we ask, why? If Barbados is somewhere about the base of the yellow fever volcano, St. George's is perilously near the brink of its crater, for it is more liable to be invaded by that disease. I was told that "a certain amount was being done." Any sanitarian knows what that means. It is a hygienic opiate which stills the conscience of officials and lulls the populace into a false sense of security. There is no use mincing words when dealing with these matters. Questions concerning life and health are, or should be, too important to be relegated to the domain of fair speech and suave excuses. The mailed fist and not the gloved hand is required when dealing with grave faults in tropical sanitation, but what with lethargy, inertia and vested interests, even the mailed fist finds it difficult to accomplish the work, and it must in any case be wielded with due tact and discretion. I speak feelingly, for I was devoured by stegomyia—the mosquito curtains being wrongly hung upon an old four-poster bed. My only satisfaction was that, like MOWGLI, I enjoyed much good hunting aided by an electric torch.

I received the same kind hospitality in Grenada as in Barbados, and hence was able to see some interesting cases. Amongst other places visited was the colony of "Poor Whites" at Mount Moritz. Canon WALTON, who takes a keen interest in these poor people, and is also alive to the claims of hygiene in the tropics, accompanied me. These settlers—some 200 in number—came from Barbados forty years ago. I need not tell you who they were originally, or how they have kept to themselves. In Barbados I had seen some of the children lying ill with enteric in St. John's parish. Beautiful children certain of them were, their fine features telling of good blood and an

ancestry at one time of high degree. I found similar boys and girls in Grenada, for the most part sturdy, well-nourished, good-looking, though pale, and fairly alert (*fig. 2*). But there were notable exceptions. Where the deadly ankylostome had fastened there was evidence of anæmia and degeneration. I shew you a small boy with the typical facies (*fig. 3*), the youthful victim of severe hook-worm disease. It was the same tale throughout. So long as these children escape ankylostome and malaria infection, there is not much wrong with them, and both mentally and physically they at least approach children of their age in temperate climates. It was another story with the adults. These unfortunate people, some, remember, with traces of blue blood in their veins, are termed "Red Legs," and are looked down upon by the prosperous negro. Amongst them I only noticed one who could be called a good type of manhood. He was rather a fine fellow, who had recently returned from Panama, and who, I think, would have compared favourably with the average European labourer of his age and race. Poverty, venereal diseases and drink play havoc with the "Poor Whites," and, of course, some are suffering from the effects of ankylostomiasis and chronic malaria. In Barbados there is not, as I once thought, "a fair field and no favour" for judging the question of the adaptability of the white race for prolonged residence in the tropics. Malaria, it is true, is absent, but ankylostomiasis is common and is specially prevalent amongst the "Poor Whites" of that colony. It is a pity something cannot be done for the children. They attend school, recite Dr. BRANCH'S "Health Catechism" in a parrot-like fashion, unaided by pictures or diagrams, and some of them shew promise. Here is an opportunity for a wealthy philanthropist to save the offspring of the "Poor Whites," and give them a fair chance in life! Considering the ancestry of some of them there is no saying what surprises such a scheme might produce. One certainly feels that—

"Some mute, inglorious Milton here may rest,
Some Cromwell guiltless of his country's blood."

The question of the "Poor Whites" leads us to the larger question of the White Race in the Tropics. Some new facts have accumulated and some fresh statements have been made since the problem was last considered by this Society. For example, CHAMBERLAIN has recorded the results of his investigations in the Philippines, both as regards the

physiological activity of Americans in these islands and the influence of tropical residence on the blood. His conclusions will surprise some of you and please others, for, as regards the first subject, he says;—

1. It seems probable that climate *per se* exercises little if any harmful influence on Americans in the Philippines.

2. By far the larger part of the morbidity and mortality in the Philippines is due to nostalgia, isolation, tedium, venereal disease, alcoholic excess, and especially to infections with various parasites.

3. The facts justify the hope that the progress of tropical sanitation may ultimately permit the permanent colonization of certain parts of the tropics.

Has the American occupation of the Philippines lasted long enough to justify these views? Will the results apply equally well to the protected and healthy offspring of Americans wholly reared in the Philippines? I cannot say, but we find similar opinions expressed by the Administrator of the Northern Territory of Australia, and by Drs. HOWSON, HOLMES and MAPLESTONE, while so great an authority as Surgeon-General GORGAS is also in accord. Moreover, here is an interesting note which I came across in the *Indian Medical Gazette* for November:—

“The possibility of a Northern European race acclimatizing itself in the tropics is one of vast importance, and especially to the inhabitants of Australia, as so much of the northern portion of that island continent is within the tropics.

“Theories are many and facts are few, therefore it is worth while here giving some details of a genuine example of an unintended experiment in this direction as narrated by Mr. J. Macmillan Brown in his recent book, *The Dutch East* (Kegan, Paul & Co., 1914).

“The story is briefly as follows:—In 1665, eight Dutch soldiers were sent by the Netherlands East India Company to the little island of Kissa, sixteen miles off the most easterly point of Timor; a fort was built and they were told to watch the Portuguese. The Company forgot all about this lonely outpost, and Sergeant Kaffyn and his men realised that they were in fact marooned. They had their wives with them; a guiding principle of the Dutch East India Company. They set to work to build houses and cultivate the land. The descendants of these eight couples still remain. They have been wonderfully fertile; in the

two and a half centuries the 16 have risen to 300, and they are a sturdy race with no signs of any evil effects from interbreeding. They still keep their blood pure and still have big families, and many have fair European faces and complexions and many children have light hair and blue eyes. These people had to work, and work hard, and the consequence is that after 250 years in this tropical island they are still fertile, indeed prolific, and still keep their North Europe characteristics."

As regards blood changes, I had an idea that possibly the pallor of Europeans long resident in the tropics, and that of the healthy "Poor Whites," was due to a certain grade of anæmia which was really a physiological and prophylactic change. The plethoric man does not usually find tropical conditions to his liking, and I fancied that Nature might possibly aid the Caucasian to withstand adverse conditions by slightly altering his blood state. If CHAMBERLAIN is correct, this hypothesis is not valid, for in his paper on "The Influence of Tropical Residence on the Blood" he tells us that his observations shewed that examination of white men after a year or more of residence in the tropics gives an average erythrocyte count well above 5,000,000, a hæmoglobin percentage between 88 and 90, and a colour index ranging from 0·82 to 0·88. For Filipinos the average hæmoglobin estimations were 93 per cent. These figures do not indicate an impoverished condition of the blood. The expression "tropical anæmia" is often found in the earlier treatises on the diseases of hot countries, and is still heard not infrequently. It is his belief that such a condition, *due to the effect of climate per se*, does not exist. More recent investigations have shewn that much of the anæmia formerly classed as "tropical" was in reality secondary to infections with plasmodia, uncinaria and leishmania.

It would seem, as MUSGRAVE and SISSON maintain, that the pallor of the skin is merely due to a local vasomotor condition, a cutaneous ischæmia.

Considerations for space forbid further reference to this interesting question, and indeed Grenada itself cannot claim much more attention. Malaria exists in its river valleys, but in Dr. COCKIN's absence I was unable to get accurate information as to the type chiefly in evidence. Endemic filariasis, as Dr. LOW has noted, an observation confirmed by Dr. COCKIN, is exceedingly rare. Why should this be so? Ankylostomiasis is rampant, but has now happily been taken in hand,

and we may look for better things. It is at first strange to find that amongst the negro population tuberculosis, and more especially phthisis, ranks first as a dealer of death. A little familiarity with the conditions of life soon makes it clear why this is the case. The negro lives in a world peopled by Jumbis and malevolent spirits. These are especially to be dreaded at night, and consequently every crack and cranny of the cabin is closed against them. Overcrowding, bad ventilation, and a natural proclivity of the negro to the disease it induces give the *Bacillus tuberculosis* every opportunity. Grenada, however, has risen to the occasion. Thanks chiefly to Dr. HATTON, a tuberculosis hospital, of which I shew you pictures (*fig. 4*), is in full swing. Few hospitals in the world can command such a site and such a view as this little sanatorium.

I visited the town of Gouyave, where I met an old Edinburgh man, Dr. O'NEALE, took some photographs of sanitary interest (*fig. 5*), and saw a very curious case of what was stated to be pinta in a coolie woman. Dr. SAMBON had seen this case when he visited the island, and I shew you a photograph he took of it (*Plate 2, fig. 6*). I doubt very much if the condition had anything to do with pinta. The white skin was so healthy and elastic that I began to wonder if the so-called coolie had not once been a European who had been stained. I cannot say, but it is certainly a very remarkable case of depigmentation. Albinism amongst the negroes is not very uncommon. Here is a photograph of what we may call a piebald family (*fig. 7*). Dr. MITCHELL, of St. George's, kindly gave me the print. In Grenada, as elsewhere, there is a large ant with urine-loving propensities. Its possible rôle as a disease carrier must not be overlooked.

A word as to the south end of the island, where there is a spot once an indigo plantation and so known as "True Blue." There the conditions are wonderfully African in type, as I am able to demonstrate, and enormous centipedes can be found, as witness the monster in the bottle. One would fain linger on Grenada as one was fain to linger in it, but the fact that from its southern extremity the distant northern mountain ranges of Iere—the land of the humming bird—can, in very clear weather be descried, brings Trinidad and its problems into mind, so we will journey to the Gulf of Paria and Port of Spain.

I landed in the latter over twenty years ago, in August, 1893, to be exact, and though in those far-off days I had not fully acquired the "sanitary eye," I think I can say that I was blessed with an enquiring one.

Hence I can testify to the great change which has taken place in that capital, a sanitary revolution due largely to the labours of Surgeon-General CLARE and some of his staff, notably Dr. DICKSON (*fig. 8*). It has not been an easy task, but already the results are in evidence, and if the same principles can be applied to the colony as a whole, Trinidad will have every reason to esteem itself a fortunate isle.

There is much I might say about this, our most important West Indian possession, for, in the stimulating company of Mr. URICH, the Government Entomologist, I ranged far and wide; collected diseased *Simulium* larvæ in the beautiful verdant vale near Arima, where the Madre de Cacao, the glorious Bois Immortel, spreads its vivid scarlet flower clusters against a sky of purest sapphire; witnessed the Atlantic combers bursting in snowy foam upon the long beach line of the wind-swept Cocal with the so-called "four-eyes" spluttering in the back-wash and defying capture; plunged into the mysterious High Woods and was thrilled and awed, as was Kingsley long ago; looked once more upon the Pitch Lake, now shorn of much of its weird beauty, thanks to clearing operations following "Yellow Jack"; visited the Leper Asylum and noted the noble devotion of the French Catholic Sisters; saw Dr. SEHEULT at work in the Colonial Hospital; and spent days prowling round cow sheds, opium dens, latrines and public urinals with Dr. DICKSON, realising to the full the truth of these words—

"Where every prospect pleases,
And only man is vile."

One is dealing with problems, however, not with prospects, so let me direct your attention to those which are, perhaps, the most interesting.

1. Why has kala-azar never been found in Trinidad, or, for that matter, in Jamaica? For many years a stream of East Indians, some of them from leishmaniasis areas, has been pouring into both these colonies. It is surely reasonable to suppose that amongst all these thousands of coolies some, when they left India, were in the incubation period of kala-azar, or were even in an early stage of the disease! Yet kala-azar has not been found. Dr. DICKSON tells me he has been on the lookout for it, but has never come across *Leishmania donovani*. Is not this curious? It is true that in the New World generally this parasite does not seem to have gained a footing. Only one case of infection is

recorded in the literature, that at Manaos on the Amazon, and it does not seem to have been introduced.

Is observation at fault, or is the insect-carrier absent? Personally, I am inclined to think the disease must be present and has not been recognised, but I saw nothing of it either in Trinidad or Jamaica, though, of course, my investigations were very limited.

2. There is a big scheme afoot for planting bamboo, as a source of paper pulp, on a large scale in Trinidad. How will this affect the malaria question there? Cut bamboos, unless severed at the nodes, leave ideal breeding places for anophelines. The hollow stem can, of course, be plugged with tar, but that would be a heavy task. Might something be done by having a cleared area round the plantation, and dotting trap-breeding pools here and there? This is at least worth thinking about.

3. Plague runs as an epizootic in rats. Can yellow fever exist as an epizootic in monkeys, and especially howler monkeys? I have already considered the possible relationship of the indigenous monkeys of South America to obscure outbreaks of this disease, and Dr. Low has replied to my hypothesis. With most of what he says I am in entire agreement, but I think that in his letter he tended to overlook the point on which I wished to lay special stress. This being so, it is perhaps better to discuss the matter at some length, as, since writing my note to *The Lancet*, I have obtained some further information of considerable interest. On my way to the West Indies, I was told by a lady, Mrs. RANDOLPH RUST, who has been long resident in Trinidad, that the old negroes there say they can always tell when there is going to be an epidemic of yellow fever in the island owing to the fact that, prior to its appearance, the red howler monkeys are found dying and dead in the High Woods. In view of MANSON'S injunction to search for a reservoir of the virus amongst some of the lower animals, this negro statement struck me as curious and interesting, though naturally one did not place overmuch credence in it.

When I reached Port of Spain this monkey question assumed fresh interest. Dr. CLARE gave me particulars about a recent small outbreak of yellow fever at Brighton, the port for the Pitch Lake in the south-west of Trinidad. Briefly this is what happened:—

One of the American engineers, engaged in oil-boring operations

arrived in Trinidad from Guanaco, on the Venezuelan mainland, five days before being attacked with yellow fever, of which he died on the fifth day of his illness. He was struck down six days after leaving Guanaco, and Dr. CLARE told us that for the last twenty-five years for which records are available no case of yellow fever is known to have occurred at that place. In my opinion this does not, of course, wholly exclude an infection acquired at Guanaco, or upon the steamer in which he travelled, although in any case the incubation period would be lengthy, but Dr. CLARE was convinced that it had not been so acquired. Mark, however, what followed. This man was employed at a spot eight miles in the heart of the dense virgin forest, at the end of a road which had recently been constructed through the leafy wilderness. In this locality red howler monkeys are known to occur. Associated in work with this man was another who had not been out of Trinidad for more than eighteen months. This second man was also struck down with yellow fever on the same day and almost at the same hour as the first case. He eventually recovered. As Dr. Low admits, it is not easy to account for infection in this case, provided the medical enquiry was adequate, which, speaking from memory, I believe to have been the case. The other cases, eight in number, two of which proved fatal, need not be considered. They are all explicable by the ordinary man to mosquito, and mosquito to man infection.

Dr. GEORGE, who carefully investigated the outbreak, attributed it to some unknown cause in the oilfields amongst the forest.

Upon enquiry I found that several people knew all about the negro belief of which I have spoken. Mr. RUST got hold of his chief hunter, who confirmed the negro statement in every particular, and said that before the last large epidemic of yellow fever in Trinidad the red howlers were found dying and dead in large numbers. Further confirmation was forthcoming from Mr. F. W. URICH, entomologist to the Board of Agriculture, an acute and trained observer, who told me that he himself had seen the monkeys lying dead, and at the time thought they had probably perished from the effects of a protozoal blood parasite. He had not, however, specially associated this mortality with the subsequent outbreak of yellow fever.

A point of possible interest is that in these High Woods a species of

wild stegomyia, called *Aedes sexlineata* exists. It is very like the known yellow fever carrier.

The two men first and well-nigh simultaneously attacked were working on an oil well at the end of the new asphalted motor road already mentioned. They spent ten hours a day on the oil fields, going there every morning from Brighton and returning every evening. In this connection it is well to remember that *S. fasciata* bites by day as well as by night. In water collections at a bungalow which stood in the clearing at the end of the road, Dr. GEORGE found *S. fasciata* breeding when he visited the place (*fig. 9*). As I have said, monkeys occur at this spot, but there was nothing to shew that they had been sick or dying.

Granting that the first case got infected in Venezuela, although there is no evidence to that effect, how are we to explain the second case?

It may be affirmed the disease was not yellow fever. In reply I can only say that both cases were typical, with jaundice and albuminuria, and that the diagnosis was confirmed post mortem in the first case, and also in subsequent cases. Could the man first attacked have conveyed an infected mosquito ashore in his baggage? This is not a very probable contingency but cannot be altogether excluded.

Was yellow fever present in a mild and unrecognised form amongst the coloured employees of the American company, or amongst the negro population? Careful enquiries were made by Drs. GEORGE and CAMPBELL, who decided that such was not the case. Let it, however, not be forgotten that some medical men maintain that yellow fever is endemic in Trinidad. Of this, I believe, there is absolutely no proof, albeit it is not an easy thing to disprove.

There remains the hypothesis I have advanced. Needless to say I do not wish to urge that the monkey, or indeed any of the lower animals, is an *essential* factor in the spread of yellow fever, but I suggest that certain obscure outbreaks like that in Trinidad may possibly be explained on such an assumption, and I submit that it is at least very desirable that the liability or otherwise of the indigenous monkeys of South America to yellow fever infection should be ascertained. Dr. AGRAMONTE, of Cuba, with whom I discussed the matter, agreed with me on this point, and it must be remembered that his unsuccessful inoculations were carried out upon Rhesus monkeys, originally natives of India.

As I said before, there may be nothing in the idea, but I am told that in certain parts of Brazil a mortality in monkeys is known to accompany yellow fever outbreaks, and certain isolated epidemics in Colombia could be explained on such an hypothesis. The wild monkey and man rarely come into close contact, but they do so now and again, as possibly in the High Woods of Trinidad, and opportunities for infection might occur.

When yellow fever raged at Gibraltar, in 1828, the monkeys, probably an African species, died in large numbers, but of course mortality amongst other animals has been noted in yellow fever outbreaks.

Still, it is an interesting fact that the distribution of the genus *Alouatta*, of which *A. seniculus* is the red howler, corresponds in South and Central America fairly closely to the known distribution of endemic yellow fever. It may be a mere coincidence, but at least it would justify the experimental work I have suggested.

We know so little about some phases of yellow fever that anything which might throw fresh light upon it would undoubtedly be welcome, and if one is careful not to change hypothesis to fact, no great harm can be done, and in some instances benefit may accrue.

As we are talking about yellow fever, I may say that I have been wondering if, during its epidemic prevalence, the employment of blood tubes, like those with which RODHAIN fed his captive tsetse flies, might prove useful. If *stegomyia* were found to feed on them greedily, there might be a smaller number of human beings bitten and hence a lessened chance of infection.

Any such scheme would have to be combined with vigorous anti-larval measures, for the provision of blood-feeds would probably tend to increase breeding operations.

The voyage from Port of Spain to Ciudad Bolivar on the Orinoco, was made on the Venezuelan river steamer "Delta." It was then that I appreciated the real reason for the notices on the Royal Mail boats, with a reference to which I commenced this paper. All through Venezuela and Colombia one finds the disgusting and dangerous habit in vogue of throwing used toilet paper on the floor or into a small wooden box on the floor, and not into the pan of the water-closet. The subject is not a pleasant one, but I make no apology for

mentioning it, for, apart from anything else, each of these countries is, like Egypt, a land of flies. In each enteric fever is prevalent, as are diarrhoeal diseases generally. Is it any wonder? The custom is by no means confined to the lower orders. One finds it practised in better-class hotels, though, of course, not by educated Venezuelans or Colombians who have travelled in the United States or Europe. I enquired how this peculiar habit had originated. It appears that the earlier types of water-closet used in these countries had very imperfect flushing mechanisms and constantly gave trouble. Distrust was thus engendered, and so it is the plumber or the engineer who was originally to blame. It is not the first time that these gentlemen have upset the sanitary apple cart!

I wish I had time to describe the delta of the Orinoco as I viewed it from the Macareo Channel, and thought of Raleigh and his sweating seamen, labouring in their clumsy boats against the mighty current. Mansonias and sundry Tabanidæ boarded us, together with the little green and vicious *Lepidoseiella*, which I was to meet and feel later both on the Magdalena and the Atrato.

At daybreak one morning I saw a family of capybaras emerge from the forest, but looked in vain for jaguars and anacondas, though the jaguar is sometimes seen in the delta, where it is common. I mention the capybaras especially, because it would seem that in certain parts of Venezuela they may act as reservoirs for the parasites of "Renguera," a trypanosomiasis of equines. At any rate, it is known that before outbreaks of this disease in horses, capybaras, agutis, aguchis, and pacas, all water-loving rodents, die in large numbers. If this supposition is correct these animals form a different kind of reservoir to the big game of Africa, which do not suffer from the infection. The condition must be more like what is met with in rats before plague epidemics.

The scenery of the Orinoco changes completely once the delta is left behind. The shores are sandy and rocky, with low hills in the background covered with bush or sparse forest. At the famous narrows, called Angostura, 236 miles from the river's mouth, one reaches Ciudad Bolivar, the capital of the large state of that name. It was formerly known as Angostura, and gave its name to the popular bitters now manufactured in Trinidad.

Ciudad Bolivar is a city set on a hill, which cannot be hid, a

picturesque spot, with much of interest for the tropical hygienist (*Plate 3, fig. 10*). The Hospital Ruiz is the centre of its medical life, and here I found Dr. FELIX PAEZ busy with his microscope and upholding the torch of tropical medicine in this somewhat remote part of the world. To him and to his colleagues, as well as to the courteous Government officials, I would take an opportunity of expressing my thanks and gratitude for much kind hospitality and assistance.

One of the problems for the sanitarian, and especially for the sanitary engineer, is how to get rid of the large lagoon which at certain seasons of the year is present on the low-lying land to the east of the town, and also how to carry the surface drainage to the river. Part of it runs on to this low-lying land, forming dirty and swampy areas where pigs love to wallow, and where vultures pick up a living.

With very little trouble, and at a comparatively small cost, Ciudad Bolivar might be made a very healthy place. At present it has a death-rate of something like 23 per 1,000, its population being about 20,000.

Another problem I encountered was concerned with the diagnosis of a peculiar disease of the nose. It did not seem to be leprosy, or lupus, or syphilis, or espundia, or gangosa. I do not know what it was, but it may be identical with a condition called Bubon de Velez, which is supposed to be confined to the province of Velez in Colombia. Dr. PAEZ shewed me cases of malarial splenomegaly and blackwater fever. There is a fine field for work in Ciudad Bolivar.

As I have mentioned South American malaria, I would remind you of the well-known fact that in Brazil and elsewhere, there is a quinine resistant strain of plasmodium. ZIEMANN thinks that this is the result of the malaria-stricken population having for a great number of years been saturated with quinine, to the action of which the parasites have acquired a tolerance. He thinks it would be a great matter to find a safe and easily administered drug which might take the place of quinine. Such a drug may, I think, possibly be forthcoming from *Nectandra cortex*, or Bebeeru bark, derived from *Nectandra rodæi*, the greenheart tree of British Guiana, which belongs to the Lauracea. It was used long ago in cases of ague, and often with success, but at times it appeared to fail, and fell into disuse. Considering our more exact methods of testing drugs, both clinically and chemically, and our improved knowledge of tropical fevers, it seems to me it merits further investigation, and

I am arranging for this to be conducted. The cattle trade of the Orinoco is a big business, and interesting from the veterinary standpoint. The quarantine station and splendid slaughter-house at Port of Spain testify to its importance.

We must, however, again get under weigh, run out through the northern Bocas, once traversed by the immortal Nelson and his battleships, touch at that unsavoury and unhealthy spot Carupano, famous only for its superb rum, look in at Margarita Island with its pearl fisheries, and then attain the mainland, creeping under the shadow of that huge Sierra which rises well nigh sheer from the rim of the Caribbean, and recalls the great sea captain, Amyas Leigh, and the romance of *Westward Ho!* There is not much romance about the modern La Guaira, a terribly hot, dusty and dirty place. Macuto, the Brighton of Caracas, a little farther east is distinctly better, but one is thankful to speed up into the clouds upon the wonderful mountain railway which is under the direction of an able and genial Scot, much interested in questions of snakes, scorpions, and medicinal plants. Three thousand feet nearer heaven we find the remarkable university city of Caracas, aptly described as "a capital of beautiful prospects and beautiful women." Here, however, we are concerned with Caracas from the medical and sanitary standpoint.

Dr. CAPRILES, Director of Civil Hospitals, proved a capable and kind guide to things clinical. Under his auspices I visited the Hospital Vargas, of which I shew you pictures, together with one of a fine monument to Dr. VARGAS (*fig. 11*), the father of Venezuelan medicine. I would, however, remind you that a greater medical name than that of VARGAS is associated with Venezuela, for in that country lived and, I believe, died the far-seeing BEAUPURTHUY, a prophet as well as a priest of the goddess Hygeia. I learned, what I did not know before, that he finally devoted himself to the study of leprosy, contracted that disease, and fell a victim to it at Cumana. If this is so, how comes it that Dr. SAMBON was able to give me the photograph of his grave (*fig. 12*) from which the lantern slide I shew you was prepared? The grave is in the Penal Settlement Cemetery, Mazaruni river, British Guiana. Was his body transferred there for burial?

He would doubtless have been glad to witness the quickening of the interest taken in sanitary matters at Caracas. There was, and is,

urgent need for it. The principal hotel, under German management be it noted, is best described as a mouldy place where the food predisposes to colic and the stair carpets might have done duty in Noah's ark. The climate of Caracas is well-nigh perfect, its site is superb. No one should die there except from old age. Unfortunately there is a very different tale to tell, simply because the authorities have in the past neglected to carry out proper sanitary measures. I have not time to go into details, but would draw attention to the peon filling water barrels from a stream! It is not, however, water which is going into those barrels, it is diluted sewage. The stream is the Guiare river, into which a great part of the sewage of Caracas runs, and the bare-legged gentleman in the stream is obtaining his supplies well below the city and the outfall.

You, doubtless, suppose that the barrel contents are to be used for agricultural purposes. Not at all. They are for watering the terribly dusty main road running out of the city to the east, a road with much motor traffic upon it. Is it any wonder enteric fever is rife in Caracas, and all diarrhoeal diseases common? Yellow fever used to be frequent, but I am glad to say is now being fought, and well fought, with gratifying results. So is ankylostomiasis, and here and in Colombia they largely use higueron, the sap of *Ficus laurifolia*, a well-known anthelmintic, said to act like a charm in trichocephaliasis. If all that is claimed for this drug be true, it is time it came into more general use. At present the latex is taken mixed with coffee. It is believed an alkaloid is present in the sap. If this can be isolated a valuable preparation may be forthcoming to take the place of thymol and beta-naphthol. Time will shew.

A few years ago Venezuela celebrated the centenary of her independence. Most of the foreign powers presented gifts. Great Britain did not, possibly because it was thought that we had given enough in the form of the famous 6,000 British legionaries, those superb veterans from the Peninsula and Waterloo, who played so great a part in freeing both Venezuela and Colombia from the Spanish yoke, and about whom precious few people in this country know anything at all. Note what Germany did! She presented a very fine and complete laboratory equipment for hygienic work. I have seen it and can testify to its excellence. What a pity it is that the German race, which has un-

doubtedly done much to further science and the welfare of mankind, has now constituted itself a scourge and a menace! We shall see it playing a different rôle in Colombia.

In the new laboratory reigns Dr. GONZALEZ RINCONES, so well known for his entomological work. I found him engaged upon the fascinating problem of how and why the *Janthinosoma* mosquito acts as a transporter of the eggs of *Dermatobia hominis*. To this mosquito the picturesque name "Aeroplane of the Macaw Worm" has been given, and apparently only the female is engaged in the transmission. Now how does the mosquito get the eggs from the fly plastered on to her abdomen? Does she pick them up haphazard, or are they carefully deposited by the mother *Dermatobia*? Thanks to Dr. GONZALEZ I am able to shew you not only a lantern slide of the mosquito, but the actual insect itself with the fly eggs *in situ* (fig. 13). I believe this is the only specimen in England, so pray be careful of it! In the private laboratory of Dr. ITURBE, I saw locusts being killed by the *Cocco-bacillus acridiorum* of Hérèlle, a most interesting and hopeful sight. It has recently been employed by BÉQUET with some success in Algeria. I cannot take farewell of Caracas without expressing my great indebtedness to Mr. HARFORD, C.V.O., the British Minister, and to Dr. GUEVARA ROJAS, both of whom smoothed the way for me on manifold occasions.

From Caracas, accompanied by Dr. CAPRILES, I journeyed in a motor car to the Lake of Valencia, 70 miles to the west, a thing I hope never to do again. The scenery was admirable, the road very much the reverse, inches—I had almost said yards—deep in sand in many places, seamed by huge ruts—I had almost said dongas—and, in places, of an amazing steepness, and with terrifying curves. I now feel rather proud that I did not take the train back; at the time, and for some days subsequently, I felt I had been a fool. When in the rear of herds of Andean cattle, one was smothered in foul dust. The driving was like that of Jehu the son of Nimshi, and as a result one flew from side to side like a parched pea in a pan, was driven violently upwards from the seat, was thrown as violently forwards, and was eventually, holding fast by a rail, forced to balance oneself in the air between earth and heaven, like the coffin of Mahomet.

All's well that ends well, however, and I shew you some pictures taken *en route*.

The Lake of Valencia presents a problem. It has no outlet; twenty-two rivers run into it, and yet it is slowly drying up. We notice here the abundance of aquatic growth closely resembling the sudd of the Upper Nile. Malaria, of a very severe type, is prevalent along the shores of this lake. The little posada at Maracay, where I stayed, was alive with mosquitoes, nearly all *Culices*.

In order to reach Colombia it was necessary to go to the Dutch island of Curaçao. I went there from La Guaira in an abominable Norwegian tramp steamer flying the American flag. It also took me to Maracaibo. Curaçao is not the least like the usual West Indian island. Its general aspect and some of its flora strongly suggest Africa. It might almost be a chip of the veldt transported to the Caribbean. This being so, I was not very much surprised to come across a flourishing ostrich farm, with a stolid Egyptian fellah looking after the birds. The capital is like a little town in Holland. I spent a long time trying to find a dirty place in it. I discovered one at last, in the neighbourhood of negro cabins on the slope of a hill, but even this dumping ground was not very bad. Everything was too dry for great offence to result. The narrow harbour, widening out into a wonderful lagoon, suggests pirates, and, indeed, there is still an old pirate house upon one of the wharves. One of the principal diseases in the island is diabetes. It seems that this may be due to the fact that Jews form a large proportion of the better-class population, and this race is known to be specially liable to diabetes. Nephritis and erysipelas are also said to be common. Curaçao, with all its virtues, scarcely suggests tropical research. It is too much of a health resort. The same cannot be said of Maracaibo, at the entrance to the huge gulf of that name—a curious little city, a fine business centre, hence full of Germans, and visited periodically by yellow fever. Forty cases cropped up shortly after I had left it. Dr. COATES COLE is a leader in the local medical life here, and holds quite a unique position. He has had great experience of severe malaria, which, let it be noted, he invariably treats by intramuscular quinine injections, and of yellow fever, in which he finds a French antipyretic—cryogenin—of great service. You will be glad to know that it is meta-benzamine semicarbazide.

He took me to the leper settlement on Providencia Island, a truly horrible place. Picture wretched people without any faces at all,

others with faces like nothing human, miserable, deformed creatures, and, alas! little patients, some just beginning to develop the disease, for the healthy children born of leper parents are not removed from the lazarette but are allowed to take their chance. White, black and yellow inmates of both sexes and all ages, there they are, wonderfully cheery in what looks like misery and wretchedness, while out in the yards the lean black vultures strut and peck. It reminded one of Kipling's Indian lepers and the crows. I have never seen so depressing a place, and yet the patients are well enough fed and, for the most part, do not seem unhappy. A few do well under energetic treatment with refined Chaulmoogra oil; the majority are doomed. The wards were ill-kept and dirty, but the devotion of the nurses is beyond all praise.

Returning to Curaçao upon the ancient tramp, I succeeded eventually in catching an Italian steamer which landed me upon the long pier at Porto Colombia. Thence I journeyed to Baranquilla, a fairly prosperous but unfinished looking town, which need not detain us. *Stegomyia fasciata* was said not to occur in the place, but I caught one the only night I was in it.

There is a saying that it is about as easy to get to Bogotá as to heaven. It may be so; certainly it is a long journey from the coast to the Colombian capital, and the worst of it is one never knows how long it will take. It may be ten days, it may be a month or more. It all depends on whether your steamer sticks fast on a sandbank or not. The Magdalena is a great and noble river, but no one can say what it will do next in the way of shifting its navigable channels. The journey took me sixteen days, but I stopped for three of them at Mariquita, in the province of Tolima, the guest of the hospitable Manager of the La Dorada Extension Railway, Mr. THOMAS MILLAR.

I would like to describe the river life, the strange food, the caimans and turtles on the sand spits, the gorgeous macaws speeding across the huge water stretch, the noisy parrots, the black monkeys in the tree tops, but considerations of space forbid. The forests are truly wonderful, but well-nigh impenetrable. The bird and insect life is fascinating, but of larger wild mammals one sees next to nothing. The heat at times was almost unbearable, and the climate is undoubtedly very trying to Europeans. Scorpions come on board the

steamers with the wood fuel. When a member of the crew is stung and has succeeded in catching the aggressor, he splits the latter open and applies its internal organs to the puncture, with, it is said, beneficial results. This is something like the custom of swallowing a snake's gall bladder in the case of a snake bite.

Among the biting flies which I collected was probably a new *Simulium*, now in the hands of Dr. KNAB. I chased a *Lepidoselaga* half the morning and failed to capture it; a spider, however, succeeded where I failed, and eventually I took both locked in an embrace which could scarcely be called a loving one. The two blood-suckers are upon exhibit.

Honda, an interesting old town, has a reputation as a good place for phthisical folk. I found quite a little colony of recovered Welshmen there, men sent out almost in a dying condition, but now doing useful work.

From Mariquita, on a plateau of the same name, a magnificent view of the Andes can be obtained. Through it courses the Guali River, coming from a region of gold mines. It is said that the red, clay-stained and sewage-polluted waters of this river cause, or rather caused, goitre, which is common in the district. When another source of supply became available, it is asserted that the goitre decreased. This is interesting in the light of MCGARRISON'S views on the subject, as is the statement that in the province of Antioquia, to which I shall presently introduce you, goitre is comparatively rare, owing to the fact that the Antioquian waters contain iodine. Certainly in Colombia the goitre problem might be tackled with advantage. The disease is more common in women. Under the flanges of the rails on the La Dorada Extension Railway, running from La Dorada through Mariquita to Ambalema on the Upper Magdalena, above the rapids, I found many so-called "Cojo" spiders, brilliant creatures with bright red globular abdomens spotted with black markings. They belong to the genus *Lathrodectus*, and are said to be very venomous. I was credibly informed that a bite from one of them had proved fatal within twenty-four hours in the case of a healthy railway peon, but I fancy their deadliness is somewhat exaggerated, though typical specimens of this genus are undoubtedly poisonous.

On the way to Ambalema one was pestered by tiny *Hippelates* flies, which constituted themselves a nuisance.

Another steamer journey brought one to Girardot, and there the hotel had a notice priding itself on its excellent sanitary condition. In order to impress this upon the visitor, there was a large earthenware bowl full of water and sunk into the soil in the patio, and the water was simply alive with *culex* and *stegomyia* larvæ. I would like to have fined the proprietor. All I could do was to deliver a mild lecture in execrable Spanish and to see the bowl baled dry.

From Girardot one climbs into the clouds by a mountain railway, reaching at one place an altitude of 10,000 feet above sea level. The sudden change from intense and steamy heat to the chill air of the Upper Andean slopes undoubtedly predisposes to bowel troubles. I have little doubt that the consequent diarrhœa is analogous to the well-known hill diarrhœa of India. The famous Sabana, a great and lofty plateau, is reached at last, and after changing trains at Facatativa, a short journey across a level stretch, reminiscent of the Lombardy plain, brings one to the quaint and comparatively venerable city of Bogotá, nestling on the lower flanks and at the base of the huge twin buttresses of Monserrate and Guadalupe. Here there is a School of Medicine, and considerable activity in sanitary work. A graduate of Harvard, and a Fellow of this Society, Dr. JOSÉ MONTÓYA, constituted himself my guide, philosopher, and friend, and under his auspices I visited the hospitals, and saw what I could in the way of tropical medicine. There are plenty of cases, many coming from the unhealthy Llanos to the south. They find their way, these poor peons, into the San Juan de Dios Hospital. Doubtless the conditions there are an improvement upon those in their own poverty-stricken dwellings, but there is no use in concealing the fact that in certain respects this large and ancient hospital is about a hundred years behind the times. The reason is not far to seek, though this is not the place to discuss it. Let it be said, however, that it is not the fault of the enlightened little party of medical men who are struggling to remedy conditions which are a blot on the escutcheon of the capital.

This hospital, which I gather is always overcrowded, dates back to 1770. In one of its courtyards stands the dissecting-room of the medical school, recalling conditions, aye and producing conditions, once obtaining in Vienna. In another I found the washing out to dry, and promptly photographed it. The tiles covering the roof of the

wash-house were of the most wonderful tints, vermilion, violet, blue, golden, richest umber, and metallic green. One of the ambulances is a Sedan chair. I saw a patient being brought to the hospital in it, and I hope it will soon be on view in the Historical Medical Museum. Patients lay in rows upon the floor of the wards. All kinds of cases were mixed up together, owing to lack of space, and despite the protests of the medical staff. One saw a victim of ankylostomiasis bloated with œdema, and hard by a wasted dysentery case straining in his misery. Enterics were dotted here and there, and altogether this hospital came somewhat as a shock. It is, however, only fair to say that, thanks to the energy and influence of Dr. MONTROYA and some of his friends, an excellent children's hospital has been erected. The fabric of a new hospital is also under construction, and though money is woefully scarce we may yet hope to see a building worthy of Bogota and of its Medical School. To the staff of that School I shall always be indebted for their courtesy and abundant hospitality, while I am under many obligations to the British Legation and its Secretary, Mr. EDGAR BOWLE.

Here are two photographs of interesting cases (*figs. 14 and 15*). I am certain they are examples of the condition known as gangosa. Now, what is gangosa? Is it a disease *sui generis*, or is it the result of yaws? At Bogotá they did not recognise the condition, and I believe these are the first cases to be recorded from Colombia proper. I understand a single case has been reported from Panama. Gangosa is another problem worthy of investigation. We will revert to it again when we reach Jamaica.

Thanks largely to Mr. WYNDHAM, the British Minister, I was able to see a good deal of Bogotá, and especially of its sanitary problems. The water supply might be better; the sewage disposal might be very much better; the milk supply is open to criticism, as when one finds a donkey with a milk-can on one side of it and a barrel for hog-wash on the other! (*Plate 4, fig. 16.*) At the same time, many of the streets are well paved with asphalt and the city is making progress. It is interesting to see the Padilla spring-water being sold in the street; strings of fish from the Magdalena being carried upon a pole; and to visit the market, which is much more primitive than that of Caracas. Bogotá itself, however, cannot be called a tropical city. It is 9000 feet

above sea level, and its climate is temperate, indeed, at times, distinctly cold and rainy. One gets a good idea of the situation by riding out to the verge of the Sabana, where the famous falls of Tequendama, thrice the height of Niagara, fall sheer in spray and thunder from the edge of the plateau to a valley bottom far below (*figs. 17 and 18*).

At this spot one finds the warm air from the lower slopes meeting the chill breath of the Sabana and condensing to form those mists of which I am able to shew you a picture. Standing thus at a great altitude, and looking out upon the Andes, we may take a medical survey of Colombia as a whole, and so I exhibit some slides illustrating the distribution of certain of the more important diseases. Professor URIBE very kindly had the maps prepared for me. Here also is the one I promised depicting the rôle of the Teuton; German officers training the Colombian army. Observe the goose-step as practised in the Andes!

I returned to the Magdalena valley, and consequently to the tropics, by the old Spanish road which runs from Facatativa to Honda. Few who have not seen it can have any idea of what it is like; paved in parts; in parts like the bed of a mountain torrent; of an amazing steepness; of an astonishing miriness once the rains have begun, as they had when I essayed it; commanding every now and then the most superb prospects—the giant snow-clad peak of Tolima soaring to 18,320 feet, the long glistening range of Ruiz, the wonderful river valley lying below one like a gigantic relief map. Mule trains still traverse the road, as I now shew you, and until recently every grand piano in Bogotá, let alone minor pieces of furniture, ascended it. Is it any wonder that for animals it is a *via dolorosa*, a highway strewn with bones?

In the primitive *posadas en route* one is apt to become infected with the spirochæte of relapsing fever, and the belief is firmly held that bed bugs are to blame. Fleas are much more in evidence than bed bugs, and here is a problem requiring solution. In some parts of Colombia a tick, *Ornithodoros turicata*, is known to be the carrier.

My objective now was the Rio Atrato towards the setting sun, so I left the Magdalena at Puerto Berrio, a terribly unhealthy spot. I will not readily forget an episode near this dreary village of vultures. There being no road of any kind leading away from the town, I had gone for a walk along the railway track and was returning, sweating at

every pore, when I saw two peons carrying between them a box slung from a pole. A person in some kind of uniform accompanied them. He was a policeman. As I passed I saw the box was open, and with somewhat of a start realised its nature. Within it, with jaw tied up, with malar bones protruding, with yellow sunken cheeks, lay what had been a man the night before. The very look of him suggested the cause of death. I enquired of the policeman and learned that dysentery had killed him. "Yes," said the official stolidly, "they are always dying here; they die like dogs and are buried like dogs." Is not this sad, with emetine upon the market? There is, however, neither an hospital nor a doctor at Puerto Berrio, although it has a certain importance and marks the beginning of the railway to Medellin, capital of the Province of Antioquia. There is a gap in the railway, and one rides or drives from station to station. Dr. HENAO, who is in medical charge of the railway itself, is, however, very energetic, and keenly interested in tropical medicine and hygiene.

In the region near Puerto Berrio various species of *Conorhinus* bugs are found, and it is possible that CHAGAS's disease exists. At Medellin I was shewn a supposed case in a boy of twelve. He was not in a febrile state, so it was no use examining his peripheral blood. I never saw such a mountain of oedema, and personally I am inclined to think he may have been an example of that curious form of nephritis in the young, which was afterwards demonstrated to me at Panama.

Medellin is a very pleasing place, unhappily and quite unnecessarily scourged by enteric. In the hospital here I saw an amazing number of undiagnosed ulcers, chiefly of the legs. There is a fine field for research in this direction. At Medellin I made arrangements for the long journey on mule back across three Cordilleras, across the mighty Cauca river, across lofty and rain-swept paramos, and finally through the dense forests of the Choco to the Rio Atrato.

This was certainly the most interesting part of my journey, and I traversed a region little known either to Europeans or to the Colombians themselves. It was only owing to the kindness of Mr. BADIAN, the British Vice-Consul at Medellin, and of Señor DON CARLOS RESTREPO, a well-known Antioquian, that I was able to get proper information and secure a reliable guide.

I started from the town of Caldas, a picturesque place full of fleas, and

journeyed by Amaga and El Provenil to the Cauca valley. The trail wound along bleak mountain flanks, descended into green hollows full of feathery bamboos and singing birds, crossed considerable streams, and, in places, was distinctly dangerous, more especially when one encountered long trains of mules bearing huge planks cut and shaped in the Andean forests. It was the reverse of pleasant to meet such potential battering-rams at a sharp angle, with a river brawling one thousand feet below, and the mountain side towering like a cliff above one.

In the Cauca region, pinta of every kind and colour is exceedingly common. It is said that one species of revenge which is practised is to give your enemy pinta through contact or infected clothes. I saw several cases of the red and black varieties of this intractable disease. The Cauca, a very fine river, is crossed by ferry, and from there onwards the journey is sufficiently arduous until the upper waters of the Penderisco and the savannah of Urrao in the San Isabella valley are reached.

In the coffee country near Concordia I took several rare *Tabanidæ*, and I killed a species of coral snake on the savannah. Urrao is an interesting upland town, or rather a church with a town attached, for the new place of worship dominates the landscape. The surrounding scenery reminded me of bits of the Clyde valley. It is a great cattle country. Redwater occurs but is not very prevalent, and ticks abound. In the Pavon valley pellagra is common. Maize is the staple food, but it is said to be of good quality. Here are running streams, and *Simuliidæ* almost certainly occur, though my search for larvæ was futile.

At Urrao I saw a case of very acute and violent mania in a pellagrin. Sanitary conditions are well-nigh non-existent, and as a result enteric takes toll of the inhabitants. Everywhere it is the same story—flies, filth, and disease.

The rainy season now began in earnest, and from near Urrao onwards I rode in drenching rain for the most part. One climbed, and better climbed, amongst the greyish-green Andean forests, very still and apparently lifeless, till the Paramo of Sumbacula was reached, in a region of extinct volcanoes. *Tabanidæ* swarmed upon the road whenever the rain ceased, and I reaped a rich harvest. As will be seen, these mountain *Tabanidæ* differ from those taken in the Atrato valley.

From the Paramo aforesaid one descended for a whole day, shrouded in mists and vapour, by a very rough, primitive, precipitous track to the

roaring torrent of the Ocaidocito, above which, upon a covered bridge, one spent the night in fair comfort, shrouded in mosquito curtains. Thereafter it was a case of struggling along a muddy and flooded forest path, now through long soaking grass, anon cutting a way with the macheté through tangled bush or dense plantain and rubber groves, meeting with wild and naked Indians, fat and comely folk of a rich bronze colour, decorated with beads and very pleased to get a few cigarettes; plunging through rapid and rather perilous rivers full of deep pot holes and swollen like the Spey in spate; catching Tabanids and Chrysops and Dichelacera when ever the sun shone for a space and cheered one up; and sleeping in empty, leaky huts, until at last we halted at Charicha on the banks of the Arquia.

It is to be noted that while the Tabanids attack the fetlocks of an equine, the Chrysops are nearly always to be found about the neck or withers.

From Charicha I descended the Arquia by canoe to its junction with the Atrato, a vast and deep river fringed by the densest tropical growth. There, thanks to the kindness of a Syrian gentleman hailing from Egypt, I was given a room to serve as a laboratory. Unhappily it rained well nigh all day and every day. The river rose and the place became a veritable swamp. There was practically no dry land on which to walk, save for a path along the side of the Arquia. Hence I had to be content with catching flies and mosquitoes, which abounded, and with making a few blood examinations.

The population is wholly negroid, riddled with syphilis, poverty-stricken and superstitious. I found a case of old nasal myiasis in a negro. It appeared that he had been cured by the use of liquid creasote, originally intended for treating cracks in calves' hoofs. Anyhow, I washed out his nose thoroughly with a mixture of milk and chloroform, but was unable to expel any larvæ. In his blood, however, I found a sharp-tailed filarial embryo, which I recognised as *Microfilaria demarquayi*. This is a new locality for this nematode. The infection was fairly heavy.

The quaint toucans, with their huge yellow bills, are common at the Boca de Arquia, and it is perhaps interesting to note that they swarm with lice, which Mr. GUY MARSHALL informs me belong to the genus *Menopon*.

Far up the Atrato the Indians obtain a poison for their blowpipe arrows from the venom of a small yellow toad about two inches in length. The venom is procured by hanging the hapless amphibian over a slow fire, when the gland fluid collects upon its cuticle. I was told that a dart thus poisoned caused slight local swelling and rapid death from paralysis. FAUST, of Strasburg, as you probably know, has demonstrated the highly toxic properties of the venom of several species of toad, so I have no reason to disbelieve this story.

After a week in this forsaken solitude, the ancient paddle-steamer passed up river on her way to Quibdo, the capital of the Choco country, some sixty miles south of the Arquia, and with a very evil reputation as regards disease. Malaria and blackwater fever are both rampant.

I embarked on the venerable "Santa Barbara" upon her return, and voyaged to the mouth of the Atrato through a wild forest land, full of egret-haunted swamps and lagoons, the home of the jaguar, the puma and the tapir, and peopled by Indians and negroes. On either hand, far back, were tree-covered slopes and hill ranges; those on the west separating the Atrato from the waters of the Pacific. Towards the mouth of the river I saw many howling monkeys amongst the bushes. Crossing the Gulf of Darien, we reached Turbo, another unhealthy place, and then, with some trepidation, splashed out to the open sea at three miles an hour. Far away we could mark the spot where the unfortunate Scottish colony came to a miserable end, largely through lack of the information which now we happily possess, and unhappily so rarely apply in a proper manner.

Touching at Zapote, where the Sinnu river pours a huge volume of water into the Gulf of Morrosquilla, we came finally to the historic Cartagena. Then, on another steamer, calling at the great banana port of Santa Marta, and remembering that banana bunches often harbour rats, I found myself one morning passing over the spot where lie the bones of Francis Drake, and shortly thereafter I was at Colon.

Dr. MALCOLM WATSON dealt so fully with the Canal Zone that it is not necessary to repeat what has been said, and, in any case, Panama no longer possesses the sanitary interest which was such a feature of the excavation days. Still, there is much to be learned at Ancon Hospital, where Dr. DARLING, Dr. CONNOR, Dr. JAMES, and others with well-known names, take every trouble not only to give you a good time, but to see

that you become familiar with their laboratories (*fig. 19*), wards and cases. Dr. DARLING has solved most of the Panamanian problems, but a few remain. I saw one case, which was said to be an example of mossy foot, under the care of Dr. CALDWELL in Panama City (*Plate 5, fig. 20*). The cause of mossy foot is still unknown. The condition is not mycetoma, which it resembles. Look at this truly appalling wreck of an Indian youth of 28 years, the victim of untreated congenital syphilis! (*fig. 21*.) Dr. CALDWELL told me that on admission he was a huge scab. Salvarsan worked wonders, but it could not perform miracles, hence this bone absorption, these scars and deformities.

The nephritis of the young negro is a curious condition. Dr. DEEKS believes it is due to toxic absorption from the bowel, the result of carbohydrate fermentation, and gives his patients plenty of butcher's meat with, he assures me, excellent results.

It is truly wonderful what the Americans have done upon the Isthmus, but there are signs of slackening, as some of their doctors admit, and it is earnestly to be hoped that the sanitary banner will be kept flying for all time. It must not be forgotten that the French did a great deal also in the way of hospital construction, but they were too early upon the scene, and paid a dreadful penalty for ignorance.

Jamaica is surely one of the most beautiful spots on earth, and yet observe what occurs there! Here is a woman with a gaping hole where her nose should be, sightless optics, and a terrible scarring upon the neck and shoulder! All this is probably the result of yaws (*fig. 22*).

Enteric is common in Kingston, and they are still worrying about the cause thereof. Is it water, is it privy-pits plus flies, is it a question of carriers and contact?

Then there is the vomiting sickness, a problem yet unsolved, despite the labours of Dr. HAROLD SCOTT, SEIDELIN, and others.

I found Major HARRISON investigating another problem, *i.e.*, the nature of the endemic neuritis of Jamaica, which is quite distinct from beri-beri, and in which the special senses are apt to be affected. Thanks to Dr. ERRINGTON KER I saw a good deal of the island, and many cases of disease, among them one of the cholecystitis, very closely simulating yellow fever. Why should a sturdy negro boy get rickets, and why, as Dr. WILLIAMS told me, do pellagrins in the asylum improve on a banana diet? Why, also, do patients in the asylum acquire pellagra? Has it



Fig 1



Fig 3



Fig 2



Fig 4



Fig 5

Illustrations to accompany Dr. ANDREW BALFOUR's Paper.



Fig 6



Fig 8.



Fig 9



Fig. 7

intention to accompany Dr ANDREW BALFOUR'S Paper.



Fig 12



Fig 11



Fig 14

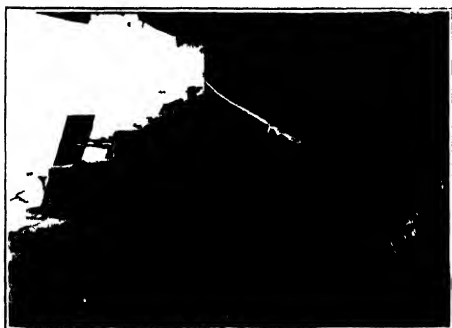
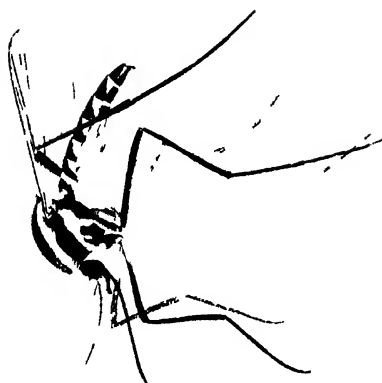


Fig 10



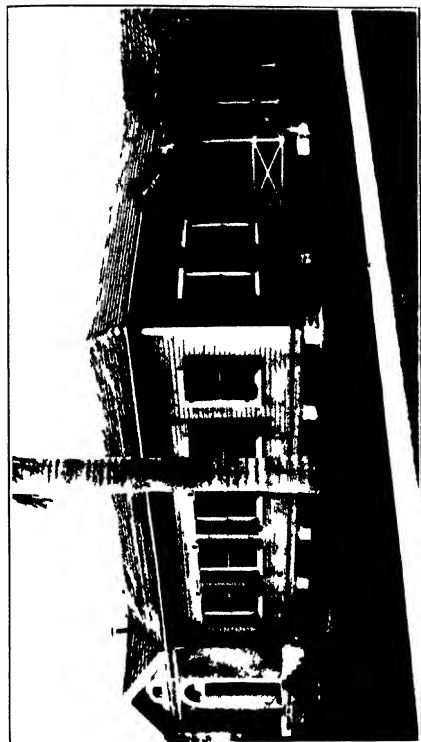


Fig 19



Fig 18



Fig 17

Illustrations to accompany Dr. ANDREW BALFOUR'S Paper.

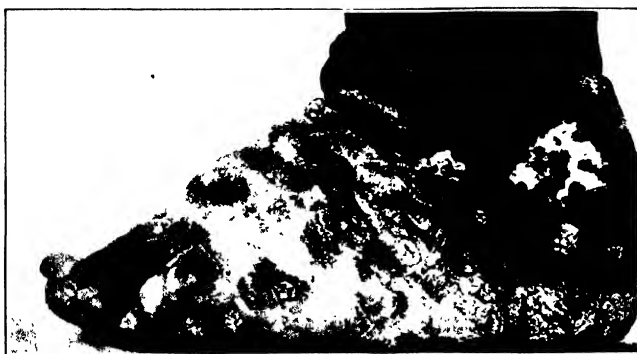


Fig. 20.



Fig. 21



Fig. 22.



Fig. 23.

Illustrations to accompany Dr. ANDREW BALFOUR'S Paper.

anything to do with the *Ceratopogoninae* on the beach, or is the *Stomoxys calcitrans* at work? Dr. MACDONALD, now busy at ankylostomiasis prevention in Grenada, gave me an insight into his sanitary problems, before embarking on yet another steamer, and setting sail for the wonderful harbour of Santiago de Cuba. Thence a train takes one right up the middle of the Pearl of the Antilles. Under American influence sanitary measures are not lacking, as witness the small boy at Camaguay Station, with his sweet-stuffs shrouded in muslin (*fig. 23*). AGRAMONTE and GUITERAS are names wherewith to conjure in the fine city of Havana, where I had the good fortune to see some cases of plague, happily for them, convalescent. I also visited the waterworks, which are one of the sanitary features of Cuba's capital.

Here, I think, we may call a halt, for we are practically out of the tropics, and between Havana and New York there remained only Nassau, in the outlying Bahamas. It is impossible with the space at my disposal to deal fully with everything that came under my notice during a tour that lasted six months.

I have only been able to give you a mere outline of my journey, but I think I have said enough to shew that these distant lands, so rich, for the most part, in their flora and fauna, are also, in many instances, rich in pathological problems, and in those conditions which destroy alike the white man and the black.

Happily most of them are preventable; unhappily many of them are not prevented. The means which should be taken to do so constitute the greatest problem of all, and yet very often it is a problem capable of comparatively easy and speedy solution. Much has doubtless been done where the British and American flags fly. At this time we remember, surely with sorrow and regret, how within a very short space of years 90,000 British troops perished in the West Indies, almost wholly from disease. An army disappeared. That could scarcely happen again, but even under the Union Jack there is need for a quickening of dry bones, for men to be up and doing, for sanitary progress, sanitary reform, and medical research. Still more is all this required in the two large Republics with which I have dealt, and which are countries of great potential wealth and of a very considerable importance in the world of commerce. The times are troublous. Peaceful Science no longer holds her sway, but when right and justice have eventually triumphed, as

assuredly they will, we may hope to see attention again directed to these lands of the west. We live in expectation of the day when mystery will yield to knowledge, and when knowledge will be applied, not for man's wanton destruction but for his comfort and salvation.

EXPLANATION OF PLATES.

PLATE NO. 1.

- Fig. 1. A pool near Hastings swamp, Barbados.
- Fig. 2. "Poor White" children, Grenada.
- Fig. 3. "Poor White" child, the victim of *Ankylostomiasis*.
- Fig. 4. Tuberculosis Hospital, near St. George's, Grenada.
- Fig. 5. Privy built over the sea, Gouyave, Grenada.

PLATE NO. 2.

- Fig. 6. Depigmentation in Hindu woman, Gouyave, Grenada. From a photograph by Dr. SAMBON.
- Fig. 7. Albinism in a negro family, Grenada. From a photograph by Dr. MITCHELL, St. George's.
- Fig. 8. Sanitary dustbin, Port of Spain, Trinidad.
- Fig. 9. Net to guard neck and part of face from *Stegomyia bites*, Dr. GEORGE, Trinidad.

PLATE NO. 3.

- Fig. 10. Street scene in Ciudad Bolivar, shewing central channel with slop-waters and blocked grating.
- Fig. 11. Statue of Dr. VARGAS, Hospital Vargas, Caracas, Venezuela.
- Fig. 12. Grave of BEAUPURTHUY. From a photograph by Dr. SAMBON.
- Fig. 13. Eggs of *Dermatobia hominis* on abdomen of *Janthinosoma luteu*.
- Fig. 14. Early case of Gangosa in a Colombian, Bogotá,
- Fig. 15. Advanced case of Gangosa in a Colombian negro, Bogotá.

PLATE NO. 4.

- Fig. 16. Milk-can and hog-wash barrel on the same donkey at the door of an hotel in Bogotá.
- Fig. 17. The Falls of Tequendama, free from mist.
- Fig. 18. The Falls of Tequendama, shrouded by the mist formed by the cold air of the Sabana meeting the hot air rising from the *tierra caliente*.
- Fig. 19. Dr. DARLING'S Laboratory, Ancon Hospital, Panama, Canal Zone.

PLATE NO. 5.

- Fig. 20. Case of Mossy Foot, Santo Tomas Hospital, Panama, R.P. From a photograph by Dr. CALDWELL.
- Fig. 21. Case of Congenital Syphilis and Osteomalacia in a Panaman, aged 28 years, Santo Tomas Hospital, Panama, R.P. From a photograph by Dr. CALDWELL.
- Fig. 22. Case of facial ulceration and scarring, possibly the result of Yaws, Kingston, Jamaica. The nasal cavity is covered by a dressing.
- Fig. 23. Boy selling fly-protected sweetstuffs at Camaguay railway station, Cuba.

Dr. D. E. ANDERSON : I should like to ask Dr. BALFOUR if he came across any cases of beriberi in Colombia?

Dr. A. BALFOUR : Yes, I did. Beriberi is quite common. There is a curious belief that it is due to drinking water contaminated by the decomposition of the wood of the ceiba, or silk-cotton, when the tree falls into the stream. Beriberi is also common in Venezuela. In Colombia it is very serious amongst workers at some of the mines.

Dr. D. E. ANDERSON : Did you see any cases of uta?

Dr. A. BALFOUR : No, I did not hear of it in Colombia?

Dr. D. E. ANDERSON : Any cases of gangosa?

Dr. A. BALFOUR : I have referred in my paper to two cases from Colombia of what appears to be gangosa.

Dr. D. E. ANDERSON : Certain authors say that gangosa exists in Colombia but not uta. I saw several cases of uta in Lima, but none in Cartagena and Baranquilla (in Colombia). Uta is often mistaken for gangosa, but according to Dr. MANUEL TAMAYO, of Peru, and other Spanish authorities, who have studied uta *in situ*, the two diseases, though resembling each other in many respects, differ from each other in the appearance of the early ulcers, and also as to the site of their origin. Uta begins as a pimple on the face; gangosa as one inside the mouth, as a rule on the palate or on the inner side of the cheek—in fact, on the mucous membrane. The deformities of feet and hands are more pronounced in gangosa than in uta.

It is very interesting to hear what you say about the so-called "Poor Whites." When I was in the West Indies last year I visited most of the British Colonies, and came across these "Poor Whites." There they mix in a friendly manner with the blacks at school and in their homes, but they are not received in the houses of the better class of white and black, and yet some of them can trace their ancestry to good European families. They are the descendants of passengers and sailors taken prisoners by the

Spaniards, and by the French and English pirates, and liberated or turned into slaves on those islands.

Dr. A. BALFOUR: I believe many of the "Poor Whites" of the West Indies are the descendants of the old Jacobites. After Sedgemoor, also, many of the prisoners were sent out and sold as slaves.

Sir RONALD ROSS: That remark about kala-azar not being present in the West Indies. The same thing holds good at Mauritius, where there are hundreds of thousands of coolies, and where no case has yet been reported. In Mauritius there is a very large medical staff, and they are very capable men, who have been constantly hunting for it. I searched, myself, about five years ago, but without success.

About the white population. There is in Mauritius a white population, which has remained there for some centuries and which is not degenerate in any way.

Dr. D. E. ANDERSON: There are few white families in Mauritius who are poor, and they are very different from the "Poor Whites" of the West Indies. In Mauritius they are the descendants of the first colonists of Louis XIV.'s time, and most of them members of noble families.

Dr. F. M. SANDWITH: I am perfectly certain that, although many of you are silent, I shall be voicing your sentiments by giving our very best thanks to Dr. BALFOUR for the great treat he has given us to-night. Amongst other things he has taught me at least, and possibly you, a lot of geography. He has sketched out some very interesting problems—clinical, pathological and bacteriological. It is interesting to see the extraordinarily good buildings provided for treating hospital people. It shews that many of the people in whose countries Dr. BALFOUR has travelled, appreciate the fact that certain sick individuals should be looked after; but the general sanitation which is so near the hearts of the Fellows of this Society is almost entirely neglected. The country is beautiful, and only man is vile. That, of course, one sees in many foreign parts, even in Europe; beautiful hospitals but an entire absence of hygiene outside them.

TRANSACTIONS OF THE SOCIETY OF TROPICAL MEDICINE AND HYGIENE.

FEBRUARY, 1915.

VOLUME VIII. No. 4.

Proceedings of a Meeting of the Society on Friday, January 15th, 1915.

SURGEON-GENERAL

SIR R. HAVELOCK CHARLES, G.C.V.O., I.M.S.(R.), *President*,
in the Chair.

BACILLARY DYSENTERY.

BY

DR. H. S. GETTINGS.

Bacillary dysentery is a disease which may be taken as an index of the sanitary condition of a community and of its powers of resistance. It is for that reason that it diminishes before the advance of civilization, and thus it is that if we trace its history in the British Isles, from being a ravaging pestilence in the Middle Ages, it gradually shrinks, both in virulence and amount until it disappears as a disease of the general population, and now is a medical rarity outside asylums.

I propose in this paper to confine myself to the dysentery of these northern climates, and especially of the British Isles, not that I wish to confine the discussion to it, but because I wish to leave the question of tropical dysentery to others better qualified than myself to deal with it.

In view of the present circumstances, I have devoted myself more to dysentery as an epidemic disease—to the causes which promote the epidemics—than I have to dysentery as an individual disease.

For it is essentially an epidemic disease, as we shall see when we follow its history, and to-day in our asylums its epidemicity is as marked as ever. We shall see how it bursts out for two or three or more

years, after which it subsides, though a few scanty cases occurring every year carry on the infection until the cycle is completed and the next epidemic crops up.

But there is another thing we shall notice, and that is the influence of the general health of the community and their powers of resistance. We shall notice how, though they may have had infection in their midst for some time, an outburst only comes when something or another has pulled them down and reduced their natural resistance. For dysentery tends to leave alone the robust and healthy, and to afflict the weakly and those below par. Exceptions of course occur, but, as a rule, this holds good.

For to dysentery, perhaps more than to any other disease, may we apply the parable of the "Sower and the Seed." We know in that how the seed which fell on stony ground was unable to take root, but that which fell on fertile soil brought forth fruit, "some an hundred-fold, some sixty-fold, some thirty-fold."

In dysentery the question of the soil is nearly as important as the question of the bacillus. Thus it was that in the Middle Ages its ravages were so much more extensive and so much more virulent than in later times. For life was much harder in those days, and though the better classes may have lived comfortably enough, yet the bulk of the community were near neighbours to both famine and pestilence. Not only was there a greater chance of getting infected through the lack of sanitation and filthy habits of the age, but their resistance was sapped in addition by the housing conditions, the poverty and poor feeding which were common features of their existence.

For it must be borne in mind that life in mediæval England was about on a par with that of much of the East to-day. The filth, squalor, overcrowding, and poverty were of a degree than we can barely realise, unless we turn to Asia. Famines came every few years as an addition to their struggles, and those of you who may have worked in India through plague and famine, have seen what life was like for the poorer classes in the England of six centuries ago.

These facts will remind us, when tropical dysentery is talked about, that dysentery has no great predilection for the tropics. But they possess the sanitary conditions which that dysentery loves and which England used to have. When the tropics attain to the sanitary level of England

to-day—both of the individual and of the community—dysentery will, I think, be correspondingly scarce.

In addition to the big epidemics of peace were its ravages in war. For from the earliest times it has marched with the armies, and merciless though the mediæval soldiers were, they could not equal the numbers dysentery laid low. Leaders fell as well as men, for it was impartial in its favour. Edward I. died of relapsing dysentery at Burgh-on-Sands, as he was preparing to invade Scotland in 1307. Henry V. died of dysentery caught at the siege of Meaux in 1421, while a few years before the army he took to France was within a few weeks reduced to a quarter of its numbers through dysentery; and he was retreating to England with the weakened diseased remainder when he was forced to turn at bay and fight Agincourt.

Time does not allow us to do more than glance at the military history of dysentery, but I should like to draw your attention to the outburst among the troops at the siege of Dundalk in 1689, as it clearly shews the influence of the seed and the soil.

In those days dysentery was so common in Ireland that it was called the "country disease." Then to the autumn of 1689 was an exceedingly wet one, when the old Dutch General Schomberg landed with 10,000 troops to besiege Dundalk. He was joined by three regiments of Enniskilliners. While he had a few well-trained Dutch and French troops, the bulk of his forces were newly-raised English battalions who were nothing but farm labourers in uniform, not one in four of whom could load and fire his simple musket. The camp soon became a marsh. The regular troops knew how to look after themselves, and their huts were warm and dry. The Enniskilliners, being natives, were used to the climate, and could make the best of it. But the English recruits failed at this, and when sickness broke out they suffered as raw troops ever do.

Raw troops cannot understand the need for the strict cleanliness, the house-maiding, the cleanliness and tidiness necessary when large numbers of men are gathered together; they do not know the little things which make the difference between comfort and misery, and they suffer in consequence. At Dundalk, without old non-commissioned officers or soldiers to shew them (for the officers were as raw as the men) their camp became a piggyery of filth and discomfort. Dysentery soon

broke out in epidemic form and 6,000 died ; so many succumbed of the sick sent on board ship for Belfast that it is said vessels lay in Carrickfergus Bay with nothing but corpses on board.

Those soldiers who had warm clothes and bedding generally escaped the disease, while it swept away in thousands those who were thinly clad and slept on the wet ground.

The next year, in 1690, Marlborough, who took an army to South Ireland, shewed that he had learned a lesson from Dundalk. He pressed everything forward and attacked vigorously ; Cork fell in forty-eight hours, and immediately the troops moved on to Kinsale, where the same tactics were repeated. What he lost in men he more than saved in time, and just as dysentery began to appear the town fell, and he was able to close the campaign and withdraw the troops.

Why I have mentioned this is because I am not aware of any great outbreak of dysentery among our soldiers in Marlborough's wars. Perhaps someone here to-night can tell us if this is correct or not. Should there not have been any severe outbreak some of the credit may be due to Marlborough, for "Corporal John" always looked after his men's health and comfort, and probably remembered the lesson of Dundalk.

Even if the army got off lightly the navy suffered in those days, for the port towns seemed to be full of dysentery and the sailors took it to sea. Anson's men suffered badly in his voyage round the world, while Smollet—who was present as a surgeon's mate—gives us in *Roderick Random* a vivid picture of the ravages that dysentery and other diseases made among the fleet at the siege of Carthage in 1741.

When the Seven Years' War came our forces suffered severely—for this time there was no "Corporal John" to look after the men. Our military were copying the Prussians at that time, and consideration for the private soldier was not a weakness of that amiable race in those days.

We suffered badly in the various campaigns of the Great War, the Walcheren expedition, for instance, having dysentery mingled with its ague. But our losses were nothing to those of the French and other continental armies. Dysentery was prominent in every campaign, though the French suffered more after 1808, which was when Napoleon,

who had shattered his old troops against the Russians at Eylau and Friedland, had to raise young troops or even anticipate the conscription. But the losses of 1812 dwarfed every other campaign. The Grand Army had dysentery before ever it entered Russia, and the sickness was enormous all the way to Moscow. Though, as may be imagined, it was nothing to the retreat, when the cold, hunger, exhaustion and depression provided the disease with exactly the conditions most suitable for it.

Let me give you a few details of the early part of the campaign from a surgeon attached to the Wurtemberg Corps.¹

In May of that year they began a series of forced marches across Poland; these, with the great heat of the days, the cold of the nights, the want of fresh water and provisions, sapped the strength of the troops before the campaign had begun and sickness began to appear before they even crossed the Niemen. The forced marches continued across Lithuania, while food got scarcer. For a long time all that they got was the meat of cattle dying of exhaustion or starvation. The men drank from any water, no matter how stagnant or foul, and the officers were unable to stop them. When rain and cold weather set in a general diarrhoea broke out, with such severity that it is stated that the route from camp to camp was marked out by offensive evacuations. The sick were in such numbers that they could not be properly attended to, and the most of them died.

At the post-mortems on these dysentery cases, in some instances the stomach was found inflamed and ulcerated as well as the intestines. The ulcers sometimes being small with dentated margins, with similar ones in the rectum, and in other cases they were larger and extending into the small intestine.

As a rule the sufferers in a dysentery epidemic are depressed and overcome with lethargy. To shew the influence of mental states the Wurtemberg surgeon says: "Of the 4,000 Wurtembergers who took part in the battle of Smolensk, few were free from dysentery. Tired and depressed they dragged along on the march, but as soon as the soldiers heard the cannon their expression changed from sadness to joy, and during the four days the battle lasted the disease vanished as if by magic. But when the battle was over it returned worse than before, and the troops fell into complete lethargy."

Leaving the Napoleonic wars, we may just notice that dysentery accounted for half the deaths in the Russo-Turkish War of 1828-29, while in the Crimean War, the allied French and English forces had nearly 14,000 cases, our first leader—Lord Raglan—also dying of the disease.

It was also to the fore in the Franco-Austrian War of 1859, and in the American Civil War dysentery and diarrhoea caused nearly one-third of the total Northern losses.

On the contrary, in the Danish War of 1864 and the Seven Weeks' War of 1866, dysentery was little in evidence. Probably because they were short, quick campaigns, with the troops on the move and without sieges and longstanding camps. Whereas in the war of 1870, with its sieges and different conditions, the Germans had 38,652 cases with 2,380 deaths, and the French—though I have not their figures by me—suffered heavier still, I believe.

In the Russo-Turkish War of 1877-78 both sides suffered severely, and at the sieges of Plevna and Kars dysentery rioted amongst besiegers and besieged. In South Africa we had 38,108 cases with 1,342 deaths.

In the present war, up to now, I believe dysentery has been exceedingly rare. Up to the middle of November I know that at the No. 4 General Hospital, at Versailles, there had only been one case with dysenteric symptoms, and even in that the Pasteur Institute had been unable to isolate the dysentery bacillus.

The reason for this, I should think, is probably due to the different conditions under which our soldiers are taking the field to previous wars. Officers and men are now trained sanitarians, and I believe that, whether in camp or the trenches, the British Army is a sanitary model to any other army of the world; and the credit for this is due to the labours of the R.A.M.C., which has now come to its own. The War Office is, indeed, getting triple value for the money that it spent and the concessions that it gave the one-timed despised Army Medical Service.

Beyond the question of sanitation—which means reduction of chances of infection—is the matter of the personal resistance of the soldier and of the care that is being taken of him.

True, he has a rough time in the trenches, but when his turn is over he is able to rest in comfort, warm and dry—perhaps with hot baths

and clean clothing as well—while the food, whether in the trenches or in camp, is excellent. Then, too, when out of the trenches the men get mental change and interest from the concerts, cinematographs, lectures, and other entertainments that are given them, and which supersede the monotony and mental depression that occurred in past wars.

Whether we shall keep as free when the new armies, with their younger, rawer troops, take the field, remains to be seen; and, too, when we may have to follow up and occupy trenches and ground used by the enemy—who appear to be suffering to some extent from dysentery.

Having followed dysentery in war, let us glance at it in peace. The further back we go in our history the more severe were its ravages, for the worse were the social conditions of the population. In mediæval times Hirsch⁹ says: “The old chroniclers, in their notices of pestilences, place it next after plague and pestilential fever.” It is really only from the 16th century that our records are full enough to get useful accounts of it. We have to get away from the mediæval chronicling of the marvellous, to the spirit of genuine inquiry and desire for facts which the Renaissance brought.

For instance, it was the 16th century before the London Bills of Mortality began to be kept, and they were not generally issued or figures given for the various diseases until 1629. An interesting point about dysentery in the general population was the regularity of its outbursts. These remained very constant, at about twenty years, from the beginning of the 17th century to the middle of the 19th century, when it disappears.

These outbursts were not separate events, unconnected with one another, but are linked together by cases in the intervening years. Wherever we are able to get complete figures we find this is so. The Bills of Mortality shew it for London, while a century’s registers and records shew it at Wakefield Asylum. After generally lasting three to five years, the epidemic sinks to a few isolated cases which crop out every year and prove that the infection persists and is being handed on. When the cycle of years is completed from some mysterious cause, another epidemic arises, and so the tale goes on.

In the case of London, the Bills of Mortality shew that the bloody flux was epidemic in 1629-30, after which the numbers sink, only to rise again in the years 1649, 1651 and 1652. Twenty years later and

we get the epidemic of 1669-72 of which SYDENHAM wrote. This we know to have been widespread in England. The next outburst was 1693-99 and raged over the British Isles. It was said to have been so severe in parts of Wales that there were houses in which there were barely one or two left to bury the dead.

We can gather from this what a pestilence it might be in those times, and the reason was largely due to the social conditions. Life was rough, coarse and uncleanly, even in the middle and better classes, to a degree that few realise to-day. The poorer classes were, of course, infinitely worse off. Even a good class house of that date had rooms without ventilation, and sanitation did not exist, for it usually had a privy in the yard near the well and a stinking cess-pool in the cellar. Those were the times when both prisoners and 'prentices prayed not to be put with itchy bedfellows. Cleanliness was little regarded, and we may have an idea of this from the complete edition of Pepys' diary. In it he records the most minute acts of his life for ten years. Yet though he notes when his head and feet were washed, if I remember aright there is never a mention of his having a bath.

Captain Dampier, who was a contemporary of Pepys, says in his voyages: "I do believe it is very wholesome to wash mornings and evenings in these hot countries—at least three or four days a week. For I did use myself to it when I lived afterwards at Bencoolley, and found it very refreshing and comfortable." His tone of apology and pride of daring mingled is also very refreshing and comfortable.

But with the passing of years conditions improved, and thus it is that as we come to the 18th century dysentery is milder in its ravages; for though the poor lived under bad conditions, yet even they were an improvement on what had been in mediæval times; and as civilisation advanced an increasing proportion of the population lived under improved conditions, and thus dysentery sank in the social scale.

The strange cycle of twenty years was clearly shewn in the 18th century with its outbreaks in the 'twenties and 'forties, the big outbreak of 1758-62 and of 1780-85. On each occasion the physicians of London appear to have been taken by surprise, so much had previous epidemics faded from their memory. Yet we know from the Bills of Mortality that deaths from the bloody flux had occurred every year. They probably happened only amongst the poor, and

though the aristocratic physicians may not have met with it, I expect the humble apothecaries knew of its presence during the lean years.

For instance, Dr. WATSON writing to HUXHAM in 1762,² says: "We have had this autumn a disease which has not been epidemic, to my memory, in London. Very few of our physicians have seen this disease as it appeared of late."

Again, there was the usual dying down and recrudescence in 1780-85, and then after that, 1800—with war time, bad harvests, high prices, and semi-starvation—saw another outbreak. In fact at the time blame was laid on the oatmeal supplied to the poor.

WILLAN,² who was at the Carey Street Dispensary, said that dysentery had not been epidemic in London from the autumn of 1785 to that of 1800. He says there had been sporadic cases every autumn, but he never saw a fatal one.

The outbreak at Millbank Prison,^{3,4} is additional to the regular epidemics, but it contains one or two interesting points bearing on the question of the seed and the soil. It was a new prison, having been opened in 1816, and though bowel complaints were common, open dysentery was rare till 1823. The year before the food ration was cut down till meat was practically withdrawn from the dietary, one ox head being boiled for soup for 100 prisoners. In March, 1823, scurvy broke out, and half the prisoners were affected. The food ration was then increased, but in April dysentery appeared, and by June 454 of the 800 were attacked. "There was every degree of flux that was ever seen or described." Finally they had to empty the prison entirely and send the prisoners to the hulks. In the end, I believe, they were all pardoned.

This is the same story that Anson's voyage told, scurvy pulling them down and dysentery following on. But there was one section of the prisoners that escaped both epidemics, and they were those who worked in the kitchens, and presumably could obtain extra food.

Two years later, in 1825, the usual general outburst came, and lasted to about 1830. Though it was widespread it was a much milder affair than what the early epidemics had been. Then in 1849 came the last general epidemic, after which it vanishes from the ordinary population. Cholera was epidemic too that year, and as a rule where dysentery had been cholera followed.

The reason of the disappearance of dysentery as a general disease, I think is largely due to the sanitary zeal and reform of the 'fifties. The cholera epidemics of 1832 and 1849 had aroused the nation to the dangers of the filthy slum and the insanitary town, and matters were so improved that the people of to-day can barely imagine the conditions that were comparatively common seventy years ago.

From a report⁵ presented to Parliament in 1842, on the sanitary conditions of the labouring poor, we find the Poor Law Medical Officers all over the kingdom reporting the presence of dysentery. In the marshes of Somerset and Bedfordshire there were dysentery, ague, and typhus. The cottages of the poor reeked with damp, and the floors were often of beaten earth. In the towns it was worse. At Bath water had to be carried a quarter of a mile, and so was more precious than strong beer; and in a Greenock street was an enormous dung heap of 100 cubic yards of solid filth; this fetched high prices, as by continually adding to it it was kept of the same age. The flies were there in myriads. In another place there was a court almost filled by a huge dung heap, which, as there was no privy, was used by the inhabitants instead, and as the blue book says: "A considerable part of the rent of the houses was paid by the produce of it." One could quote much more if time permitted. However, all these conditions were swept away, and with them went dysentery, after its long reign.

But it still remained in the English asylums, and to-day there is more dysentery there than in most of the armies of the Great Powers. For instance, the top figures of the French Army were in 1906, when they had 1,217 cases; in 1909 they had 137.

The English asylums had 1,457 cases for 1911¹⁰ = 313 deaths.

"	"	1,155	"	1912 = 287	"
"	"	1,159	"	1913 = 270	"

and it does not seem to be diminishing; apart from the epidemic fluctuations, the figures to-day are as bad as they were ten years ago.

Taking the figures back to 1903, there has never been less than 10 to 12 per 1,000 attacked each year, while the total morbidity has never been less than 3 per 1,000. This means over 10,000 cases in the last 10 years, so that English dysentery is far from extinct, and the problem of its presence in our asylums is no small one.

I have been able to trace out the dysentery history of Wakefield

Asylum since its opening in 1818, and it is an epitome of dysentery in the country at large. Introduced almost immediately the place was opened, it has lingered there ever since, and the asylum has never been freed. There have been a series of epidemics from 1825 to the one which has given us nearly 300 cases since 1911, and these have been linked together by the cases in the years between. I have been able to trace dysentery in all but nine of the years, and those not consecutive ones, since the opening 96 years ago.

Some of the epidemics have points of interest. As far as I know—and the case books for those early days are wonderfully kept—no patient was admitted with dysentery in 1825, and yet in that year the dysentery present in the asylum broke out in epidemic form at the same time as the epidemic began in the country generally.

The same thing happened in 1849—no introduction, yet it became epidemic just as outside. The present epidemic began at the end of 1910. The first months of 1912 were free until the coal strike of that spring, when they had to reduce the heating of the wards, and a fierce little epidemic began almost immediately.

Sanitary measures of all kinds have been adopted at Wakefield to clear it of dysentery, and have uniformly failed. Drains have been tested and relaid, while sanitary alterations of all sorts have been made; water, food, milk, etc., all have been attended to and the source changed, and all without avail; and the reason is that carriers are responsible and not sanitary defects. They hand the infection on and originate the fresh cases and epidemics, and until they can be detected the disease cannot be eradicated.

Scotland proudly claims that her asylums are free from dysentery—and outbreaks are certainly rare. The reason, I believe, is that they do not have the enormous numbers congregated in one asylum that they do in England. The Edinburgh asylum—Morningside—has, I believe, about 500 patients, whereas Wakefield has 2,200, and there are others with even more. Then, too, the Scotch asylums claim they go in more for fresh air treatment than the English ones do. They say that they give their patients a more natural life with less restrictions, and therefore their resistance is far better. Whether this is so or not I cannot say. My work lies in the laboratory and not in the ward.

But—and this is an interesting point—outbreaks do occur in

Scotland if the conditions become less favourable. At Morningside in 1902, and at Woodilee in 1911-12, epidemics occurred. In both instances overcrowding was present, thus shewing that the infection was actually there, and only wanted less healthy conditions to arise to manifest itself.

BACTERIOLOGY.

With regard to my own bacteriological findings I have little to announce. Much of my work is incomplete, for the war has deprived me of my laboratory assistant, and I am working under difficulties at present.

In 1913, the crest of the wave of the present epidemic, I obtained a FLEXNER's bacillus from half the cases I examined, whereas in 1914, with the epidemic shrinking, my percentage dropped to less than 30 per cent.

The bacilli isolated, though constant towards glucose, mannite, dulcitol and saccharose, are very variable towards sorbitol, maltose and other sugars. Bacilli, isolated from the same case, will differ one from another on these points, and if the tests be repeated will give different readings a second time.

Though this is in accord with the experience of most workers, yet some have considered differing reactions to mean different bacilli, and have in their results given tables of classes of differently reacting dysentery bacilli. An American worker—BUTLER,⁶ of Manila—took a different line and held that the bacilli were constant, and the different reactions were due to the sugars inverting.

However, by plating out pure cultures derived from single colonies on to MACCONKEY's bile salt maltose agar, I was able to obtain plates which contained colonies of both maltose fermenters and non-fermenters, and so it was clear that the bacillus *did* vary, and that differing reactions do not necessarily mean different bacilli.

Another point was the occurrence of a few cases of dysentery, apparently not due to the *B. dysenteriae* but to other organisms. I found MORGAN's No. 1 once and *B. proteus* twice. The MORGAN bacillus is interesting, for though generally the cause of epidemic diarrhoea, it is capable occasionally of giving rise to more severe symptoms. MORISON and CHITRU,⁷ at the All-India Sanitary Conference in 1912, in reporting on diarrhoea at Poona, said that MORGAN's bacillus

had been isolated from sixteen cases, six of whom had dysenteric symptoms. Moreover, in a letter which I have had from Dr. THOMAS ORR, M.O.H. for Shrewsbury, he tells me that when he was at Wakefield in 1909, as Assistant Medical Officer of Health for the West Riding, at the request of one of the medical officers at the Asylum, he examined the stools from a ward epidemic which was clinically indistinguishable from the other dysentery outbreaks. He did not obtain the dysentery bacillus at all, but got instead MORGAN'S No. 1 from nine out of the thirteen cases. No other non-lactose fermenters being present.

Other work which I have been engaged in—such as the serum relationships and reactions of the dysentery bacilli I have isolated—is unfinished, and I am unable at present to bring it forward.

I am trying to detect the carriers if possible, for if we could but get at them it would be an easy task to stamp out dysentery from the Asylum. If it were possible to obtain some test to which they would respond the task would be lighter, but there is no such test at present. A Widal is no use, for instead of being constant as in typhoid, it is fugitive and irregular in dysentery. Moreover, the different strains of the FLEXNER group have different serum relationships and reactions which further complicate the question.

Clinically these lunatic carriers are difficult to detect, as they frequently give no symptoms and do not appear to suffer from any illness. Yet they may be in an infective state all the time.

The numbers in the asylum are so great that a bacteriological search of the stools is almost an impossible task, while to complicate it the excretion of the bacilli, by the chronic cases, appears to be very irregular, and days may go by without it.

Yet until we do get at the carriers in our asylums there will not be much real progress made towards a reduction of the dysentery.

SOURCES OF INFECTION AND PROPHYLAXIS.

We may consider these together and the problem differs according to circumstances. In asylums or armies in peace time it is worth while to seek for the source of infection, and to try to cut it off at the fountain head. As it is we generally have to take precautions in

the dark. Like spies in a community, we do not know who is dangerous and who is not.

But frequently it is not possible to search for the source—in war time for instance—and then efforts must be mainly directed towards stopping up all possible channels of infection. On this matter I do not quite see eye to eye with last year's Lettsomian lecturer, who holds dysentery to be largely water-borne, whereas to me water is only one of many other sources of infection. The fæces of the dysenteric contain the bacillus, and what the fæces soil there the infection lies. It may be water, it may be the soil of a camp, it may be food, it may be tins, or cups, or dishes—anywhere, in fact, that the dysenteric fæces can leak or drain or be distributed or carried to, is a channel of infection.

Before I finish I would like to draw your attention to one point, and that is the persistency with which the disease may cling to a place when it has once got a hold. I have shewn you Wakefield, where it has retained its hold for 96 years, and JOB⁸ points to the Châlons Camp, where epidemics have persisted from Napoleon's days. For LARREY dealt with the dysentery there in the first years that the camp was occupied, and it continues to reign there to-day.

Finally, we shall bear in mind the dangers that any lowering of the resistance of the community may entail.

How it may be the exhaustion and poor feeding of war, as shewn by the Wurtembergers. It may be overcrowding, as at the two Scotch asylums. It may be underfeeding, as at Millbank; or it may even be ordinary cold, as in the Wakefield epidemic of 1912. But whatever it is, if the seed be present it will give it its chance of settling on soil that will be fertile for it and of bringing forth fruit "an hundred fold" and more.

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DISCUSSION.

Dr. F. M. SANDWITH: I am afraid almost all my views, which are quite in accord with the speaker's to-night, have lately been published, but I should like to add to your own words, Sir, the gratitude of this Society to Dr. GETTINGS for giving up the tranquility of his northern laboratory to come here, at short notice, and give us such an interesting paper. It is impossible for our thoughts now to be kept long away from the War, and as the speaker has already mentioned the soil and the seed, it may be apposite if I remind the Society of the Belgian and French soil on which our troops are fighting at the present time. I suppose that everyone who was acquainted with that heavily-manured soil before the War could not be surprised at the cases of tetanus of which we have heard, because we know now, if we did not then, that the civil population suffered endemically from tetanus. Since the war began we have been expecting the possibility of typhoid fever. I am glad to say, among our own troops, so far as I know, there have only been some 400 cases. That is not so with other armies. I do not know the number of cases among the German troops, but I am told it is excessive, and there are certainly about 4,000 cases at Dunkirk, chiefly among the French soldiers. Certain arrangements have had to be made to-day about it.

With regard to dysentery, there are two dangers for our troops at least. One is the possibility of infection in France itself from the existing civil and military population. The other is from exotic carriers, who are very likely to be met with anywhere after they have been ill themselves. They may have reached France from India with our troops, or from North Africa with our French allies. The prevalence of dysentery in the French Army, apart from the colonies, has been much higher than in other European armies, judging by the statistics which Dr. JOB gives between 1903 and 1907. The number of cases, as Dr. GETTINGS has said, diminished very successfully from 1,217 in 1906 to 137 in 1909. In

addition to the fact that dysentery hangs about camps, as he has told us, there are also certain regiments which suffer out of all proportion to others. For instance, the French 98th infantry regiment had, in 1906, 109 cases of dysentery; in 1911 there were 14 cases in the same regiment. The great probability is that these cases were conveyed by carriers, as Dr. GETTINGS has stated. It is also important to note, and with this Dr. GETTINGS is in accord, that although dysentery is usually diagnosed in the summer, ten per cent. of this same regiment, in 1905-1906, who were suffering from diarrhœa, agglutinated the bacillus of dysentery between November and June; that is, carriers were continuing their nefarious trade of transmitting the disease, which in winter was called diarrhœa, and in summer was called dysentery. Fortunately, we know that epidemics where the SHIGA bacillus predominates are more severe than those where the FLEXNER type is the chief one.

One word, if I may venture on it, as regards prophylaxis. We all know how men think of carrying out ordinary rules for the prevention of disease in war time. We assume the sanitary authorities are doing all they can to protect the water. In regard to epidemics, on the other hand, I think all sporadic cases are due to carriers, and Dr. GETTINGS may be right that carriers are more responsible than water, and our early cholera experience has perhaps misled us on that point. Certainly, the only safe rule is to suspect any case of diarrhœa which occurs in a patient who has just lately suffered from dysentery. I have seen three or four in the last week. If possible—I do not know how far the military authorities would say it was possible—every dysenteric case should be kept isolated in hospital, and should be retained for a fortnight after all symptoms have disappeared. That is only because most bacilli apparently lose their virulent activity in twelve to fourteen days. Some carriers, on the other hand, as in asylums, are probably able to convey infection for much longer, probably months. Then there must be scrupulous care of latrines, which the soldiers would not be likely to think of for themselves, and they must be taught the importance of washing their hands after every motion, and keeping the clothing unsoiled as much as possible. These are details which the soldier, uneducated on these points, is not likely to think about.

We come to the other question, which Sir ALMROTH WRIGHT and others are working on to try and prepare a stock serum of the type or types—it

would very likely be a mixture—which are most likely to be encountered, so that when our troops or allies suffer at all severely from dysentery we may have a stock of serum at hand to treat them with. I am afraid to say anything about the prophylactic vaccine because I have no experience of it. Possibly other Fellows of the Society may be able to tell us whether the writers who have committed themselves to paper on the subject are justified in recommending prophylactic vaccination, which healthy men might take in order to be protected from bacillary dysentery.

Professor W. J. SIMPSON: I would also like to add my congratulations to Dr. GETTINGS on the very interesting and instructive paper he has given us, and for the historical information—which, I am sure, is new to many of us—in which he has entered into the details connected with dysentery epidemics. I think scurvy had a great deal to do with the dysentery that affected the Army and Navy during the earlier European wars. In regard to Anson's voyage round the world, in which he lost four-fifths of his crew from disease, a very large proportion of them was due to scurvy and the dysenteries that were associated with scurvy. It was, as Dr. GETTINGS has said: the soil was prepared by the scurvy, and then the dysentery bacillus had its opportunity of attacking the patient.

I am of opinion that although there was a very large number of cases of dysentery in the South African War, that much of its mildness was due to the fact that the commissariat was good. I am inclined to think that the immunity from dysentery in the English Army is due to the good feeding of the troops carried out by the Army Service Corps, powerfully assisted by the sanitary arrangements which have been so admirably carried out by the Royal Army Medical Corps. In fact, I think that owing to that good feeding a very large amount of dysentery has been prevented. If one considers the campaign of 1812, it is evident that hunger and privation helped materially to cause high mortality. I place great importance on good feeding in the prevention of disease.

I also agree with Dr. GETTINGS' remark in regard to clothing, chill, and other secondary causes which he has mentioned. I think they help largely, but I do not agree with him in his view of the water not being one of the principal causes in campaigns in regard to dysentery. I saw a great deal of this disease in South Africa, and it was associated, so far

as one could ascertain by enquiry and investigation, very largely with the non-purification of the water. As soon as the troops began drinking the water of the Orange River, the Modder, the Vaal, the Eland and the Crocodile, which were exceedingly muddy, and contained a large amount of mineral and organic matter in suspension, those regiments which did not purify the drinking-water were not very long before they were attacked with diarrhoea, which soon, if they continued to be in that locality, ended in micro-enteritis, and large numbers of the soldiers of these regiments were attacked with dysentery. Similarly when any of the pickets of the different armies got to these rivers, and drank the waters without purification, they were attacked with dysenteric diarrhoea. There were similar instances in the campaigns in Afghanistan, where a regiment going up one side of the river had purified its drinking-water taken from the river, and another regiment on the other side had taken no precautions. The regiment which purified the water escaped dysentery, while the other was attacked with the disease; and then when the same precautions were taken in this latter regiment the dysentery disappeared.

I agree with Dr. GETTINGS, however, that there are other causes, such as infection by hands and boots and carriers, and there is no doubt that flies had something to do with the prevalence of dysentery as well as enteric fever in badly-kept camps; and I fear, as he does, that with these newly-formed regiments going to France and elsewhere, especially when the spring and autumn come—at the time when it is the season for dysentery to prevail—that a very different state of things to that now existing may present itself. One noticed a marked difference in the condition of camps of volunteer regiments and of regulars in South Africa. It was possible to tell immediately one entered a camp whether it was one belonging to the regulars, or to European regiments that had been in India, or to volunteers, British and Colonial. The camps of the latter were exceedingly insanitary. Those of the regulars were, as a rule, clean; while the camps belonging to regiments from India, and accustomed to campaigns, were by far the most sanitary. They had learnt to be very particular about the cleanliness of their camp, and the importance of purifying their drinking-water to avoid cholera, and this stood them in good stead in South Africa against dysentery and enteric fever.

As regards the prevention of dysentery, I think that it is a matter of

organisation very largely—and of sanitary organisation. Purify the water and make arrangements for detecting the localities in which the first cases occur, so that measures may be taken at once to combat the disease before it spreads and is carried to other camps or infects other passing troops. This necessitates attention to statistical returns, not of regiments as a whole, for they may be divided up, but of localities in which there are troops. If the statistics are classified together as belonging to a brigade or division or army corps, it is likely that from them it might appear at head-quarters that there was very little dysentery, and that it was negligible and not needing special measures to prevent extension, whereas if the statistics are based on localities as well as regiments, the distribution would indicate a serious state in some camps, with a tendency to spread to others, and freedom, or comparative freedom, in the remainder. I think it is very important for the regimental doctor to grasp the importance of knowing the distribution of the disease in his camp and among the troops under him, and, besides dealing with the suppression of the disease, sending a statistical return to head-quarters.

As regards vaccines and vaccination against dysentery, I was hoping to learn something from Dr. GETTINGS on that matter. My difficulty lies in the fact that so many bacilli are derived from dysentery of different strains, and the question is which strain we shall have to vaccinate with to prevent disease.

I would again like to express my very great pleasure in listening to Dr. GETTINGS' paper.

Dr. D. R. ROBERT: I have seen no dysentery during my work with the French Red Cross in Northern France. We had 100 beds in our hospital, one third of which were occupied by Colonial troops. We were always on the look out for dysentery, but never found it. We did, however, amongst the French and Colonial troops find many cases of mild diarrhoea due, I think, probably to exposure and fatigue. These cases would clear up within three or four days after entering hospital, that is, when the men were thoroughly rested up. The French hospitals suffer from lack of excellent nursing, such as the British Army orderlies and nurses are able to give. The French Medical Authorities isolate their cases of typhoid, dysentery, and so forth in

separate hospitals, and in that way lessen the chance of an epidemic assuming large proportions.

Dr. G. C. Low: Before the discussion ends I should like to ask Dr. GETTINGS some questions, not from a critical point of view, but purely for my own information:—

1. Is the dysentery in the asylums limited to any special type of patient in the asylum? Is it in the old and weak or also in the young and strong?
2. How long does a patient excrete the bacilli after clinical symptoms have disappeared?
3. Has Dr. GETTINGS gone into the bacteriology of the different diarrhoeas?
4. Do these cases of bacillary dysentery relapse?
5. What is the best treatment for them?

The PRESIDENT: Before calling upon Dr. GETTINGS to reply, I desire to make a few remarks. With regard to prophylaxis, it seems to me the prevention of dysentery is the whole thing, and the prevention of dysentery means cleanliness. If you want to protect the outside of your body, the covering of your body, from animal, vegetable, mycotic parasites, or bacillary attacks, you are careful with regard to your bath and your clothing. Now it seems to me that if you take all that trouble with regard to the outer covering of your body, why not pay attention to the inner lining. So long as the inner lining is kept clean, so long as the cells of the inner lining are capable of carrying out their vital functions, generally it may be said it does not matter what parasite enters the body, that parasite will be killed.

In speaking of India, I have always said that it is what you eat and what you drink, more than the climate, that kills Europeans. What is simply an indiscretion in diet, and punished simply as an indiscretion in England, is a crime and is punished as a crime in India as regards errors in consumption of meat and drink.

My personal experience certainly contradicts the view of the lecturer on the danger of impure water. During the time, almost two years, in Baluchistan, Afghanistan, and Turkestan, I was in

charge of a field hospital, and had a considerable number of troops. It was borne in upon me there, undoubtedly, that bad water produces dysentery, and I still believe it does. After my first year in India I did not use a filter, but I always boiled the water. No dysentery or bowel troubles were ever in my house. At the same time I may say that no cold food was ever used.

I have had a considerable experience on the Medical Board with regard to dysenteric cases. In this last seven or eight years many hundreds of cases have come before me, and it is very interesting to cross-question these officers on what happened to them, and the various forms of treatment they have gone through. Some of them have suffered from laboratory methods, some from surgical methods, and some from the physicians. From laboratory methods I have known patients being under treatment going on for weeks and fortnights, receiving the serum injections. During all that time no directions had been given with regard to diet or clothing. With regard to the operating table, I have known the colon to be removed for dysentery, but the patient was not cured. Very recently, as my friend Dr. Low can testify, a patient had an appendicostomy performed, and he was warned to keep it open for at least another year. Well he was cured by emetine, and he need never have had that surgical operation performed. Now this makes one think of the Hypocratic axioms. The physician must not only be prepared to do what is right in himself, but also to make the patients and the attendants and the externals co-operate. Many of these officers would be saved in pocket and pain of body and anxiety of mind if those in charge of them remembered what Hypocrates wrote.

I might here draw attention to another matter—I am afraid I am rather changing the subject from bacillary dysentery, but I cannot at the same time refrain. I must congratulate Dr. SANDWICH on his Lettsomian Lectures; but I wish to draw his attention to an error. He puts it down there that the use of ipecacuanha was revived by Sir PATRICK MANSON. While at Netley, in 1882, I was taught by Surgeon-General MACLEAN the use of the drug, and during my work in Afghanistan, in 1884-86, I had considerable experience in prescribing it, for we had much dysentery. My confrères of the Indian Medical Service had not given up the use of ipecacuanha. In making the

statement that Sir PATRICK MANSON resuscitated this valuable medicine and restored it to the profession Dr. SANDWITH somewhat overstrains the question. I should like Dr. SANDWITH, when he brings out a second edition of the Lectures, to see that fair play is done.

The point made by Dr. Low a moment ago is a very pertinent one—that referring to the condition of the patients affected by dysentery. They are of dirty habits and their nutrition is poor. Both of these conditions are probably strongly influenced by their mental state and defective innervation.

I will now ask Dr. GETTINGS to kindly reply to the criticisms made by the different speakers.

Dr. H. S. GETTINGS: If I reply fully to Professor SIMPSON I think I shall cover the points raised by Dr. SANDWITH. With Professor SIMPSON I am in entire agreement except as regards the question of the disease being water-borne. I must admit I have no experience of epidemics during campaigns abroad where water is the main infecting agent. But I know that in our asylums water plays no part. Nor, if one can go by the history of the disease, was water the main channel in England in the olden times. I do not regard the disease as a true water-borne one. To me infection by water is evidence of recent faecal contamination. I felt rather baffled by Professor SIMPSON's account of the two regiments and the river in Afghanistan, but he provided the evidence I wanted as to the disease being due to local infection, by his later account of statistics *versus* geography in South Africa.

Professor W. J. SIMPSON: I added afterwards, when purification of the water was carried out by the regiments on the other side of the river, they were both free.

Dr. H. S. GETTINGS: Certainly, but in South Africa I think you said that statistics based on Army classification—brigades, divisions, etc.—might shew a very low dysentery rate on account of them being split up, whereas one based on localities might shew the men stationed at certain places to be suffering excessively.

Professor W. J. SIMPSON: I think I shewed it was due to the non-purification of the water.

Dr. H. S. GETTINGS: Quite so. But it seems to me that the geographical distribution shews that it was also a matter of local infection of the water. I am afraid I have not made myself quite clear on this point. I am not questioning at all the view that water is the chief channel of infection in these campaigns. What I question is whether that entitles us to regard the disease as a water-borne one. An infected person passes the dysentery bacilli, and if there is any flaw in the sanitary chain, contamination may occur which may affect various channels of possible infection to others. It may be water, it may be soil, or latrines, or flies, or food, or it may be, as in asylums, largely direct infection, and it seems to me we are in error to label the disease water-borne and so tend to overlook these other channels.

With regard to Dr. Low's questions. First, as to the class of patient attacked. As a whole they correspond to what I have said in my paper. It depends on their resistance, and so the cases are more numerous among the old and feeble than among the young and strong. I remember a case belonging to the latter group that was rather interesting. A patient who had worked in the asylum laundry for years and had never been known to have a day's illness, was absolutely struck down by acute dysentery and died in three weeks. At the post-mortem I found the acute attack was on the top of a chronic one, and that instead of having the disease three weeks, three years was more like it. That is how carriers occur and spread infection.

Occasionally the medical and nursing staff are attacked, but the numbers are small. For instance, in 1913, when there were 1,159 cases in the English asylums, four only of these were among the staff.

The second point was how long the patients excrete the bacilli after the symptoms have gone. It is not very long; as a rule the excretions of the bacilli seem to disappear very quickly. Of course a certain proportion keep on excreting, and I had one case of a patient who had never been known to have dysentery, but she had loose motions for about four years, otherwise, as far as I know, there was nothing to draw attention to her. For some reason or other the Medical Officer became suspicious and asked me to examine the stools. I examined once and found nothing. I examined a second time, and out of my plates the only two white colonies turned out to be the dysentery bacillus. For over four years that woman had been carrying infection,

and she had apparently been responsible for originating several ward epidemics.

The fourth question concerned relapses. We have had quite a number of these, though I cannot say much about the excretion of bacilli during them as the nursing staff take it as one case and do not send me a fresh specimen. Lately, however, I have received specimens from some of the first patients I examined two years ago, and who have again shewn symptoms, here the results have been positive.

Dr. G. C. Low: It is generally supposed that bacillary dysentery does not relapse.

Dr. H. S. GETTINGS: I understand that ours do clearly enough.

Dr. G. C. Low: South African cases were supposed not to relapse.

Dr. F. M. SANDWICH: Asylum cases do relapse, but outside cases do not.

Professor W. J. SIMPSON: African cases do not relapse.

Dr. H. S. GETTINGS: As far as asylums are concerned they do relapse, though there is the question of infection a second time, for the cases are kept afterwards in dysentery isolation wards.

As regards the question of the bacteriology of the diarrhoeas. No matter whether the cases were clinically dysentery or diarrhoea, if I secured non-lactose-fermenting bacilli from them, the dysentery bacillus was present in all but a few cases.

One interesting point about this has been that I have had a few cases, perhaps half a dozen, in which the infecting organism has appeared to be a "dirty lactoser," that is, one which neither leaves the lactose peptone water alone, as the non-lactose-fermenting bacilli ought to do, nor turns it red, like the commoner coli group, but instead turns it a dirty yellow, sometimes quite discolourising the litmus. I could not find any reference to them in the literature, nor was I able to obtain any information about them from other workers. For though they were acquainted with them, they all appear to have regarded them as common weeds among the

intestinal flora and thrown them on one side, so I had to find out what I could for myself. I was luckily able to enlist the services of my friend, Dr. C. J. LEWIS, of the University of Birmingham, who gave me considerable assistance.

It was a question of whether these bacilli were truly intermediate in their reactions between the commoner coli group and the rarer non-lactose-fermenters, or whether they were modifications of either of them. Were they coli with aspirations, as it were, striving to rise in the bacillary social world, or were they non-lactose-fermenters that were going to the bad? This last was found to be the correct answer. They were non-lactose-fermenters with low tendencies. Amongst these unusually reacting bacilli I found FLEXNER, MORGAN No. 1 and *B. proteus*, and I learned that I could not afford to neglect the "dirty lactosers" in my work.

I have no experience of vaccines, as my work has been directed to the detection of the dysentery bacilli and the study of their properties. And this, I think, will have to be fully done before vaccines can be satisfactorily employed. The true relationships and consequent classification of the dysentery bacilli need determining, or else we cannot be sure which strain the patient is infected with and which we are administering.

I cannot say much about treatment either, for I have nothing to do with it. I understand, that salines are most in favour. An interesting point about this was that ipecacuanha was used very largely by the visiting physicians at Wakefield Asylum, nearly a century ago; then it seemed to become less and less in favour, and finally dropped out, though I have found a record of its use as late as 1871, which was during Sir J. CRICHTON-BROWNE'S superintendency.

Why was it that ipecacuanha was used for European dysentery, and why was it abandoned? It was introduced to Europe about 1660, and to England soon after SYDENHAM'S time, and was greatly in favour, yet we know it is no use for bacillary dysentery.

Dr. G. C. Low: Amœbic cases have been described in France.

Dr. H. S. GETTINGS: It was used extensively in England.

Dr. G. C. Low: Possibly some of the English cases were also amœbic. I agree that in pure bacillary cases it does no good.

Dr. H. S. GETTINGS: It was recommended and used largely by the physicians of the eighteenth century for the ordinary English dysentery.

Dr. C. M. WENYON: Is it amœbic dysentery? It is possible these Wakefield cases were amœbic. Cases that relapse sound as though they were amœbic.

Dr. H. S. GETTINGS: I must confess I have not examined for the amœba.

Dr. G. C. Low Where is the ulceration chiefly?

Dr. H. S. GETTINGS: In the colon. Chronic cases often shew it most in the rectum. In virulent cases the inflammation goes up the small intestine as well.

LIBRARY NOTES.

Under this heading we propose to review recently published works sent us for that purpose, and a short notice of any other works presented to the Library.

A fifth edition of that popular and useful work, *Lyon's Medical Jurisprudence for India*, is now to hand. Written by Surgeon J. R. LYON, of the Bombay Medical Service, and published in 1888, the work quickly reached a second edition in 1889. In 1904 a third edition was published, and Dr. LYON having then retired, the new edition was revised and brought up to date by Lieut.-Col. L. A. WADDELL, I.M.S. The fourth and present editions (June, 1909, and August, 1914) are the work of Lieut.-Col. WADDELL alone. The present volume runs, with the index, to 867 pages, and is very well illustrated. All its pages have been thoroughly revised, and in great part rewritten, in order to bring it fully up to date, while fresh matter has been introduced, and several rearrangements have been made to secure convenience for reference. A special chapter upon Biochemical Tests for human blood-stains, contributed by W. D. SUTHERLAND, I.M.S., the leading expert on the subject in India, is included. As the author states in his preface, all the climatic difficulties experienced in carrying out this test successfully in India have now been effectively overcome by this method. He also states that by means of Col. SUTHERLAND's form of Precipitin Test, it is now practicable for capable operators in India to use this test for the determination of human blood in suspected stains with as absolutely certain and trustworthy results as in Europe. This, of course, is a very important matter. The author also acknowledges the very valuable aid rendered throughout the Chemical section by Dr. E. H. HANKEN, D.Sc., Chemical Examiner of the Upper Provinces. Some of this observer's own special tests and improved processes, namely, his modification of STAS' process for the separation of alkaloidal poisons, his test for seminal stains under the decomposing conditions of the Indian climate, and his special test for cocaine—a poisonous drug which is now extensively employed as an intoxicant in India—are included. Sir E. R. HENRY, G.C.V.O., C.S.I., has also kindly allowed the author the use of several

illustrations and other material from his monograph on Finger-prints. All these additions help to make an already admirable book even better, and for a country like India, with its special climatic conditions, the work is invaluable. That it has run to five editions indicates how useful it has been ; and, in conclusion, all that one need say is that it will remain the standard text-book for Medical Jurisprudence in India for many a day to come. Lieut.-Col. L. A. WADDELL must again be heartily congratulated upon the excellence of this latest edition.

TRANSACTIONS
OF THE
SOCIETY OF TROPICAL MEDICINE
AND HYGIENE.

MARCH, 1915.

VOLUME VIII. No. 5.

Proceedings of a Meeting of the Society on Friday, February 19th, 1915.

SURGEON-GENERAL

SIR R. HAVELOCK CHARLES, G.C.V.O., I.M.S.(R.), *President*,
in the Chair.

THE WAR AND CHOLERA.

BY PROFESSOR W. J. SIMPSON, C.M.G., M.D.

The great war, which has brought into conflict ten Powers, and is likely to bring more before it is finished, is an event which has been and is likely to continue to be pregnant with medical problems.

The fierce battles that distinguished the commencement of the war resulted in an enormous number of men being wounded and consequent strain on medical organization and hospitals. The nature and septicity of the wounds inflicted by modern weapons have taxed the ingenuity and skill of the surgeon, and given him much to ponder over in regard to treatment. The continuance of the campaign through an exceptionally wet winter with its mud and its water-logged trenches, the flooded low lands of Flanders and the nerve racking effect of incessant gun fire have offered opportunities to the physician for study and treatment of a variety of diseases, the types of which differ in many respects from those common to civil life.

The absence of scurvy, with its accompanying dysenteries, and the comparative freedom of disease of an epidemic form which the armies have so far enjoyed are remarkable when compared with previous wars.

The immunity in this respect is a matter for congratulation, and is a tribute to the excellency of organization and efficiency of sanitary measures which have been one of the conspicuous features of the war. It would be a mistake, however, to consider that the first six months is a certain index of what will happen during the remainder of a long war, with its changing personnel and conditions, for the problem of the health of the armies is a very complex one, and includes numerous factors possessing singly and together an undetermined value. The season of the year at which the war began, the stimulus and excitement of great battles with their alternating successes, and the efficiency of the commissariat in the supply of food and suitable clothing, are not without their influence in the maintenance of health and the quiescence of epidemic disease. The armies of Germany and Austria will be in a very different physical, mental and material condition in August and the autumn of 1915 or 1916, from what they were in 1914, when victory appeared assured to them. Should epidemics then arise they will not be confined to the particular armies that are first stricken, nor will the civil population in the devastated areas escape.

Let us glance for a moment at some of the conditions that will be favourable for the development and spread of epidemic disease. Scarcity of food will add to the hardships of the civil population that have the misfortune to be within the fighting zone, for in this great siege war the destruction of crops and cattle will place large areas much in the position of besieged towns in olden days, while the rise in the price of food stuffs all round, from the disturbance of ordinary economic conditions, and from the fewer people left to till the ground, will weigh heavily on the poor in every country engaged in the war. The many millions of men in arms must be fed. Their main supply will come from their own country, but they will also take what they can get from the invaded countries.

This generation in Europe has been so accustomed to regular supplies from overland or sea by the quick transit afforded by steam power and undisturbed agricultural pursuits, supplemented by a world commerce, that the famines, dearths and scarcities of an earlier period have been forgotten. Now Central Europe is back, more or less, to a time of isolation plus war on a gigantic scale. The effects of droughts and floods, which assumed importance in times of greater isolation of

countries, have under modern conditions been counterbalanced by an inrush of produce from other lands, so that the third partner of soil and seed, viz., meteorology, has been assigned of late a very secondary position, which could only continue while each country has the world to draw on. When this ceases, as it has done for some parts of Europe, meteorology assumes its old sway. The winter, so far as it has gone, has been a particularly wet one, not only at the seat of war but outside of it. In one respect it has been an advantage, because of filling the wells, but the wet season and the purposely flooded lands of Flanders will render the conservation of food stuffs more difficult than under other circumstances, will accentuate the dearth of food in Europe, and add to the threatening destitution and want. The severe earthquake in Italy, with its 24,000 deaths in one district, will not be without its effect on the physical and mental condition of those in the immediate outskirts of this disaster and who have been subjected to the shock.

A combination of war, flood and earthquake, ending in famine in some localities and in scarcity of food in others, is calculated to be a powerful force favouring in due season the manifestation and spread of epidemic disease, whether it be typhoid fever, small-pox, cerebro-spinal disease, cholera, dysentery, malaria, or plague, should the germs of these be present and be conveyed from place to place by any of the armies or refugees.

CHOLERA INVASIONS OF EUROPE.

Sir WILLIAM OSLER dealt with typhoid fever which is endemic in those parts of the country covering the main seat of the war, and dwelt on the value of inoculation, by which the resisting power of the soldier to this disease could be raised; Dr. GETTINGS gave us a paper on dysentery; and I have been asked to deal with cholera, which is not an endemic disease in Europe or the Mediterranean littoral, but which, nevertheless, from the peculiar circumstances connected with this world-wide war has to be borne in mind and provided against. Although cholera is not an endemic disease in Europe, its visitations in the 19th and 20th centuries have destroyed millions of the population. There have been nine invasions of Europe in a little over 80 years. They have varied considerably in their duration, power of diffusion and severity;

the more lengthy ones being distinguished by important recrudescences. Certain localities in Russia, in the neighbourhood of the Caspian Sea, have been so frequently attacked, that it is a question whether the disease has established an endemic centre there as it has done in the Far East, in Java, Indo-China, and the Philippines. Although these endemic centres are in themselves a potential danger, it is doubtful whether any of them have hitherto given rise to any considerable diffusion of the disease beyond their own boundaries. The source of the nine invasions in Europe, which have corresponded with similar invasions of the countries in the Far East, has generally been traced to India, though not directly, but indirectly, by spreading by land and sea eastwards through the neighbouring countries. On nearly every occasion there has been more than one avenue into Europe, the disease travelling along the chief trade or pilgrim routes in the Near East, and radiating in many directions, but there has generally been one principal gateway by which the epidemic has entered Europe, although almost simultaneously there were often others. The interesting and informing reports of the late Drs. NETTEN, RADCLIFFE and BARRY, and now of Dr. BRUCE Low, of the Local Government Board, form a valuable record of the later epidemics.

The first pandemic of 1817, in its travels westwards, reached Astrakhan in Russia, in 1823, but went no farther. Its diffusive power, for some reason with which we are not acquainted, had spent itself. It was certainly not from any precautions that were taken. The second reached Astrakhan in 1831, but, more vigorous than the last, continued westwards across the northern continent of Europe and arrived in Northern America in the course of two years from its appearance in Astrakhan. It spread over the whole of Europe and disappeared in 1837. The third reached Astrakhan in 1847, traversed Europe by much the same routes as that of 1831, and reached America at the end of 1848. In both continents it was widely prevalent in 1849, and continued in scattered and localised outbreaks until 1851, when it subsided in Europe, except in Poland, where it recrudesced and subsequently spread to the western provinces of Russia, and down the Vistula to Prussia.

Before the subsidence of this recrudescence, it was reinforced by the fourth invasion, which reached Astrakhan in 1852, and spread over Europe and America, causing in 1854 the most widespread and fatal

epidemic that had afflicted these two continents. After a severe recrudescence in 1859 it disappeared.

The fifth entered Europe by quite a different route from the four first. Instead of *via* Astrakhan it came *via* Constantinople and the southern ports of Europe, introduced in June and July of 1865 by vessels arriving from Alexandria, Egypt, having become infected by returning pilgrims from Mecca. From the southern ports of Europe it dispersed itself over Europe and reached America and Guadeloupe towards the end of the year. The epidemic manifested itself in Western Europe and America until the end of 1868, when it disappeared from these but still lingered in parts of Russia, and during a recrudescence in that country it was imported afresh into France and Germany in 1873 and then finally disappeared.

The sixth arrived in Europe *via* Egypt or the Suez Canal, entering by Marseilles and Toulon in June, 1884. It spread over Europe, chiefly affecting Spain and Italy. Spain lost in 1884 and 1885 no fewer than 180,000 of its people, and Italy about 50,000. For the rest of Europe the extension was very limited and its nature comparatively benign. It reached South America in 1886 and prevailed there extensively during 1886 and 1887. It disappeared from America and Europe at the end of 1887.

The seventh entered Baku, in Russia, in 1892, and spread over Europe, and it was in August there was the great outbreak in Hamburg, when nearly 17,000 of the inhabitants were attacked and about 9,000 died. With recrudescences and fresh local outbreaks it continued in Europe until 1896, when it disappeared.

The eighth arrived at Baku and Astrakhan in the autumn of 1904, but did not become epidemic in Russia until 1907, increasing in force in 1910, when it caused 100,000 deaths in that country, after which it rapidly declined. Beyond Russia, Italy was the only other country in which, in 1910 and 1911, it assumed epidemic proportions. Before the epidemic completely died out a ninth occurred, several parts of Turkey-in-Europe being reinfected by fresh importations from Asia Minor by Turkish troops, and the disease has manifested itself in several parts of the Balkan States, Austria-Hungary and Russia to the present day.

The table gives a short summary of these events :—

Epidemics in Europe.	Principal Entrance gate into Europe.	Interval between each invasion in years.	Number of years continued in Europe.	General characters.
1823	Astrakhan	—	Less than a year	Did not travel farther west than Astrakhan. The Persian and Turkish armies, which were at war with one another, suffered severely.
1830-37	Astrakhan	7	7	Severe and widespread. Very virulent among the Russian and Polish troops. The war was believed to be the great cause of the rapid propagation of cholera in Europe. Great epidemic among the pilgrims at Mecca.
1847-52	Astrakhan	10	6	Severe and widespread. Invaded a larger area of the world's surface than that of 1830-37, and more deadly. Epidemic at Mecca.
1852-59	Astrakhan	nil	8	More severe and widespread than previous epidemics. On its way through Persia it attacked violently troops of the Shah. Cholera affected the troops in the Crimean War. In 1859 it attacked the French troops in Algeria and the Spanish troops in Morocco.
1865-68. Lingered in Russia till 1874	Constantinople and Southern ports of Europe	6	10	Severe but more limited in diffusive power.
1884-87	Marselles and Toulon	10	4	Less severe and limited.
1892-96	Baku	5	5	Less severe and limited.
1905-12	Baku and Astrakhan	9	8	Comparatively mild and limited.
1912	Constantinople	—	—	Mild and limited. Prevailed among the Turkish, Bulgarian, Greek and Servian troops.

EUROPEAN WARS HAVE GENERALLY BEEN FREE OF CHOLERA.

Cholera was unknown to Europe until after the Napoleonic wars, so that these were free of the disease.

Notwithstanding the number of invasions of cholera since 1823, there

have only been three wars in Europe coincident with its presence in the area of hostilities. The first was the Russo-Polish war in 1831. Cholera was very virulent among the troops, and was believed, by the medical men at the time, to have been materially assisted by the war in its dissemination over Europe. The second was the Crimean war, when cholera prevailed over the whole of Europe; and the third was the Balkan war. Cholera was conveyed to the Crimea in transports from France, but it already prevailed in the Russian and Turkish armies. Both the French and the English armies suffered, and it also affected the fleets. The *Timandra*, carrying sick from the Crimea to the Bosphorus, lost twenty the first night from cholera, and between forty and fifty *en route*. The *Britannia* lost one hundred and fifty men from cholera in ten days. The most important manifestation in the Balkan war was the outbreak behind the Chataldja lines, where it is estimated there were about 18,000 cases. It was conveyed from there into the Bulgarian army, which spread it among the civil population, through which it passed, and finally the Greek and Servian armies were affected.

I have already stated that the war in Poland was believed, at the time, to have added much to the spread of the disease; but the Crimean and Balkan wars were of a local nature, differing in this respect from the present war.

The Egyptian war of 1882-3, though not in Europe, was short in duration and practically over before cholera appeared in Egypt, so that the army of occupation suffered but little, while the civil population lost, in 1883, some 50,000 of its inhabitants.

PRESENT POSITION OF CHOLERA IN RELATION TO THE ARMIES.

The danger of cholera prevailing in the zones of hostilities next August is not a remote one. The present position may be gathered from a glance at the map, which shews the vast range of the conflict, with the chief centres of hostilities, the countries from which the troops are drawn, the invaded areas, and the countries from which cholera prevailed in 1914. In Europe, cholera prevailed in 1914, in Russia in the Province of Podolia; in Hungary in no fewer than fifty-three different centres; in Austria in thirty-nine centres; in Germany in ten, and in Turkey in two. In Asiatic Turkey there were two centres on the Black Sea. There is no information about Persia or Arabia, but they are seldom free

of cholera, especially during the seasons of the pilgrimages. War will not stop the pilgrimages to Mecca and other holy places.

There is every probability of the existing infections in Europe recrudescent, and although they possess the character of having stayed their time, had it not been for the wars of the past two years, yet there is a risk of them acquiring an exaltation in their strength and powers of diffusion by attacking a population enfeebled by hardship and destitution.

There is also always the risk of Turkish, Russian and Indian armies bringing from the East to Persia, Egypt, and Europe, a new and more potent infection, endowed with greater virulence and capacity for spreading than that of 1913 and 1914.

Moving armies are much in the same position as pilgrims and other crowds travelling from place to place. In the Indian armies the long voyage, the excellent ships they come in, and the sanitary precautions taken reduce the risk of importation by sea to a minimum, but even here "carriers" of cholera infection are not totally excluded when thousands have to be transported. The same favourable conditions do not exist on the land routes in Persia and Asia Minor, or wherever the Asiatic troops of the Turks may march. Their condition approximates more to that of the pilgrims. The one hopeful feature against the chances of fresh importation on a large scale is that there are at present no signs of an advancing epidemic from the East. On the contrary, the indications are rather that if there had been no Balkan war, cholera would have disappeared from Europe for a time as it has done in former invasions. That, however, does not justify neglect of precautions and in not being thoroughly prepared for every contingency.

MODES OF TRANSMISSION OF CHOLERA.

One of the most potent factors in the dissemination of cholera from place to place and country to country in times of peace, is the movement of crowds connected with commerce, labour and religion. The great Hindu pilgrimages in India, and the great Mahomedan pilgrimages to Mecca and other sacred shrines, are active agents in the spread of cholera in epidemic form. Many Indian investigators have demonstrated their influence. Some of the exceptional festivals are attended by millions from nearly every part of India, but even the smaller ones are powerful in disseminating the disease, especially those held in the endemic area,

such as at Calcutta and Puri. I remember the great outburst at the Ardhodaya Jog, in Calcutta, in 1891. It is a festival that occurs every 37 years. Cholera broke out at the festival, and on the return journey of the pilgrims I was able to trace the spread of cholera from village to village through which the pilgrims had passed, and the setting up of local epidemics in the villages on the return of the pilgrims to their homes. No disease has had its extension from place to place so thoroughly traced to the lines of human intercourse as cholera. The influence of the Mahommedan pilgrims from different parts of the world to Mecca is well known. Mecca has played a part in most epidemics as a great disseminating centre. In 1883 I had the opportunity of demonstrating that two factors had played the chief rôle in the outbreak of cholera at Damietta, the first town attacked by cholera in Egypt in the epidemic of that year. One was the importation of the disease by pilgrims returning from the Hedjaz, and the other contamination of the river water from which the inhabitants drew their drinking water. The investigation merely confirmed the discovery of SNOW in 1849 and 1854, as to the mode of spread in England, and that it was applicable also to Egypt.

So much is known to-day regarding the transmission of cholera that it will hardly be realised that thirty years ago there were acute controversies on the subject. When I first went to India, in 1886, BRYDEN'S theory of cholera being earth-born and carried by the winds was held by the Sanitary Commissioner with the Government of India, and there were many followers of the same school; the comma bacillus was scouted as the cause of cholera; and MACNAMARA'S views were hotly contested, although he had proved by an accidental experiment that the dejecta of cholera patients in water produced cholera, and that cholera was spread in India by human intercourse and by the drinking of water polluted with cholera dejecta. The late Colonel DUNCAN, I.M.S., had his career spoilt for opposing the views of the Sanitary Commissioner. It was only in the Presidency of Madras that the teaching of Professor PARKES held sway. KOCH'S discovery of the comma bacillus in cholera patients in Egypt, and subsequently confirmed by him on his visit to India, gave a precise method of determining the medium by which the disease spread. KOCH found the comma bacillus in a tank in Calcutta. Later, in that town, during my administration, it was a matter of routine when an outbreak occurred to ascertain which tank or pond contained the bacillus and which not. It

added precision to the inquiry and to the preventive action that followed. At certain seasons of the year cholera bacilli were found in the Hooghly, and in the unfiltered water supplied to the town for bathing platforms and other purposes. In epidemics in Europe it has also been the practice to examine suspected river waters, and often with success. Similarly, as milk was diluted with water from the tanks, the bacillus was often found in the milk. Among Europeans the chief danger from cholera and typhoid fever in Calcutta was the drinking of contaminated and unboiled milk. In an investigation made by HAFKINE and myself into the etiology of the cholera bacillus in nature, and the results of which were recorded and read by us in a paper at the Indian Medical Congress, held in Calcutta in 1894, we demonstrated that out of forty-six tanks around which cholera existed, comma bacilli were found in forty-two, or 91·3 per cent.; and out of five tanks where cholera had disappeared a month to six weeks previously, comma bacilli were not found in any. This latter conformed to a common experience that if a tank was guarded for three weeks or a month, and further contamination with cholera dejecta prevented, the water was safe to drink. Of fifteen wells examined, nine of which were in cholera infected houses, comma bacilli were only found in one; other agencies were at work here. The air of infected rooms was examined and no commas found, even when the body of the deceased had not been removed and the floor of the hut had been soiled with cholera excreta. In a flour shop, a man attacked with diarrhœa had washed his clothes in a tank behind the premises, and we discovered his clothes still wet lying on a portion of flour exposed for sale. From the flour we obtained a culture of the comma bacillus. Cholera bacilli were also found in the surface drains inside infected houses, and also in the drains leading to tanks.

But comma bacilli were not confined to the waters of the Hooghly or Tolly's Nullah, or the canal in the suburbs of Calcutta, or to tanks or drains. I had frequently observed a marked coincidence between outbreaks of cholera with diarrhœal disease among calves in the neighbourhood of tanks. This led us to examine cows and calves suffering from diarrhœa in the vicinity of cholera outbreaks, with the result that commas were found in the intestines of fatal cases, especially of calves. We also found comma bacilli in the cesspools connected with the cowsheds in which animals were suffering. The

exact connection of these commas to cholera in man we had no opportunity of determining. Further, in some fish examined by me, I found comma bacilli. Similar observations were subsequently made by CUNNINGHAM, REMLINGER and NOURI.

That flies can transport cholera bacilli, which become adherent to the surface of their bodies, was demonstrated by GRASSI, CATANI, TIZZONI and SIMMONDS at an early period. The experiments of SAMTCHENKO, in 1893, in the Kiew laboratory, shewed that cholera micro-organisms could live and multiply within the bodies of flies. Both observations suggested the possibility of contamination of food and the indirect spread of cholera by flies.

In 1894 there was an outbreak of cholera in the Gaya Jail, and Dr. MACRAE, of the Indian Medical Service, traced it to the drinking of milk contaminated by flies from a neighbouring latrine. HAFFKINE isolated the comma bacillus from the milk.

Since the epidemic of 1892, at Hamburg, it has been frequently observed that persons who have been in contact with cholera patients, or living in infected localities, may have cholera bacilli in their intestinal discharges although they are perfectly well and never have had cholera. They are in the same position as persons who have been in contact with diphtheria and get lodged in their throats the diphtheria bacillus, which is harmless to them but dangerous to others.

A certain percentage of those attacked with cholera become chronic "carriers." Early observers have examined the bile of fatal cases and established the fact that the cholera bacillus in a certain percentage of cases is to be found in a pure culture in the bile. Major E. D. GREIG, I.M.S., in 1913, confirmed these observations by investigations he was making at Puri during the pilgrim festival there. Out of 270 post-mortems he found cholera vibrios in the gall bladder in no fewer than eighty cases, and they were not only on the surface of the mucous membrane, but also in the submucous tissue. This fact brings cholera into the same category as typhoid fever as regards the production of chronic cholera carriers. But cholera becomes even more closely allied to typhoid fever in its modes of dissemination when two very important facts, discovered and established by Major E. D. GREIG, are taken into account. The first is that out of fifty-five cases of cholera he found the comma bacillus in the urine of eight

of his patients, and in two of these cases the bacillus was recovered during the stage of convalescence, when the persons were going about their work. The other important fact is that he has found cholera bacilli in the lungs and other organs of some fatal cases of cholera.*

PREVENTIVE MEASURES AND ANTI-CHOLERA INOCULATIONS.

With cholera introduced into the war area, and its capability of spreading by "carriers," by water, and by food or drink contaminated by infected stools or urine, by infected latrines and flies, contaminated boots, clothes, utensils, and hands, there is, when the season of the year and the condition of the population are favourable, a strong probability of much loss from this disease, and it is because of this probability that measures should be at once taken to prepare to combat this disease, and to protect the troops against cholera in Asia Minor, Egypt and Europe.

It is obvious that disinfection of the latrines, and the protection of water supplies or purification of water, are essential parts of any preventive measures. So is the isolation of the sick and the retention of convalescents until free of cholera bacilli in the fæces and urine. The disinfection of the latrines is necessary to prevent the contamination of flies which crowd to these latrines, and to prevent contamination of boots, etc. But as the conditions of warfare often render this difficult, if not impossible, and what may be done in our army may not be done in another, so that the one that takes precautions may suffer owing to neglect on the part of the other, it is important that the soldiers should be also protected by inoculation against cholera, if that inoculation renders them less susceptible of being attacked by the disease.

There can be no doubt that the very extensive experiments with HAFKINE'S prophylactic against cholera, which were carried out in India on man and not on laboratory animals, twenty years ago, established the fact that these inoculations gave a very high protection against cholera attacks for at least one year. The experience gained in the cholera experiments was the guide to the preparation of the well-known HAFKINE'S prophylactic for plague, which has proved such a boon to communities attacked with plague. As most of the cholera vaccines—except those used in Upper India—were prepared in my laboratory at Calcutta, and as I had to collect the statistics relating not only to the

* *Indian Journal of Medical Research*, Vol. I., 1913.

experiments in Calcutta, for which I was responsible, but also with reference to the inoculations in different parts of India, in order to report on the subject, I can speak from experience as to their value. HAFFKINE and I received very valuable help from my assistants, especially Dr. R. SEN, Dr. J. N. DUTT, Dr. S. B. GHOSE and Dr. J. J. CHOWDRY, who not only took a very keen interest in the investigation, but also did some excellent work in connection with it. The only disappointing result was connected with the first experiment, when, as a matter of caution, the soldiers of the East Lancashire regiment were inoculated with only weak vaccine in small doses: after the lapse of fourteen months from the time they were inoculated, cholera of a very virulent character attacked the regiment, but even under the unfavourable conditions mentioned, viz.: fourteen months since the inoculation, the use of weak vaccines and small doses, and the type of the attacking cholera particularly virulent, the inoculated suffered to a less degree than the non-inoculated, thus:—

640 non-inoculated soldiers had 120 cases (18·75 per cent.) with 79 deaths (12·34 per cent.).

123 inoculated soldiers had 18 cases (13·55 per cent.) with 13 deaths (9·77 per cent.).

As regards all the other experiments, whether among prisoners in jails, or coolies in camps or tea gardens, or among the general population in the bustees of Calcutta, the protection was of a most marked character. But it was observed that, as a general rule, the period of immunity did not last for more than fourteen months.

It would take too long to give you all the results recorded, but they are to be found in my Annual Report for 1896, and a much fuller account, with details, are given in HAFFKINE's paper on *Protective Inoculation against Cholera*, published in India in 1913. I shall give you those of Calcutta and of the Cachar tea gardens.

Seven thousand six hundred and ninety persons were inoculated against cholera in twenty-seven months, mostly in those bustees, or collection of huts, in which the poorer people lived, and which were usually visited by cholera year by year. Every effort was made by persuasion to get half the members of the hut inoculated. In some cases we were successful in this respect, in others not. We inoculated in

the huts and then waited events. A complete register, with all details relating to each of the inoculated and the non-inoculated in the hut, was carefully kept, and when a case of cholera was reported investigations were immediately made. Our efforts were greatly aided by an incident which occurred in one of the bustees, which drew the attention of the public to the inoculations. Two fatal cases of cholera occurred in Katal Bagan Bustee, in a population grouped round two tanks. This outbreak led to the inoculation of 116 persons out of 200 residing in the bustee. After the 116 cases were inoculated, nine more cases of cholera, of which seven were fatal, and one case of choleraic diarrhœa, appeared in the bustee. All these ten cases of cholera occurred exclusively among the non-inoculated portion of the inhabitants which formed the minority in the bustee. The following facts, among others of a similar nature, were then observed :—

In Ramdhun Dutt's house, six members out of eight in the family were inoculated between the 31st of March and the 7th of April. On the 9th of April cholera affected one of the members of the family, who subsequently died. This death occurred in one of the two non-inoculated, the six inoculated remaining unaffected.

In Shaik Subratee's house there resided fourteen persons. Two cases of choleraic diarrhœa occurred among them. After this seven out of the fourteen were inoculated. Later one case of choleraic diarrhœa occurred in an adult not inoculated.

In Karam Ali's house, the family consisting of eight members, three were inoculated on the 31st of March, and on the 7th of May one of the five who were not inoculated was affected with cholera and died.

In Munglo Jemadar's house a fatal case of cholera occurred on the 29th of March. On the 31st eleven members of the family out of a total of eighteen were inoculated. It so happened that cholera, again breaking out in the house, attacking four persons, three of whom died, *selected four of the seven not inoculated*, while the eleven inoculated remained perfectly free.

In the twenty-seven months cholera visited seventy-one houses, in which inoculated and non-inoculated persons were living in the same households, and the following table shews the days on which cholera occurred among the non-inoculated and inoculated :—

Amongst the uninoculated members, after — 1, 2, 3, 4, 5,
 and among the inoculated of the same households, after 0, — 2, 3, 4,
5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30,
 114, 118, 119, 120, 129, 132, 139, 143, 162, 189, 191, 203, — 240,
 219
251, 271, 281, 284, 300, 309, 318, 319, 334, 356, 359, 362, 370, 372,
378, 383, 384, 389, 391, 393, 394, 401, 404, 408, 416, — 433, 446,
 421
448, 453, — 472, 493, 498, — 673, — 720, 723, 724, 730, —
459 512 688 735
 and 738 days.
 and 738 days.

During the first four days after the inoculation, cholera occurred among the inoculated and non-inoculated, though in a smaller degree among the inoculated; after the first four days, there was a period of over a year when there was almost an absolute freedom among the inoculated, while among the non-inoculated in the same houses, cases were occurring during the whole year; after fourteen months cases began gradually to reappear among the inoculated as well as among the non-inoculated.

Including the occurrences of cholera in the inoculated during the first four days, the results for the whole period were as follows:—

654 uninoculated individuals had 71 deaths (10·86 per cent.), while
 412 inoculated in the same households had 12 deaths (2·99 per cent.).

The figures shew that notwithstanding the incomplete protective effect of the first four days, and the gradual disappearance of the resistance in those inoculated with doses of weak vaccines only, which a number of the inoculated people received in the earlier days of the experiment, the mortality among the inoculated compared with that of the uninoculated was in the proportion of 1 to 3·63, giving a reduction of mortality of 72·47 per cent., or in other words, where inoculations were performed, and which were subsequently visited by cholera, there occurred for every eleven deaths amongst the uninoculated, three deaths among a similar number of inoculated.

Even in regard to the first four days it was found that the mortality among the inoculated was 1·86 times smaller than among the non-inoculated, and that after that period the inoculated acquired a protection which, for a year at least, rendered them twenty-two times safer than the uninoculated. In HAFKINE'S pamphlet on *Protective Inoculation against Cholera*, and which covers a larger number of observations in Calcutta and a longer period, viz., thirty-three months instead of twenty-seven, he found that the number of deaths among the inoculated during the first four days was 1·39 times smaller than among the non-inoculated, and that during the period of immunity lasting 412 days or 14 months, the number of deaths among the inoculated was 15·79 times smaller than among the non-inoculated. It was also noticed that in bustees, where large numbers were inoculated, and which usually suffered from cholera, there was in many instances an exceptional freedom from the disease.

Gradually, as more experience was gained, the attenuated vaccine—Vaccine No. I.—was given up and Vaccine No. II., the fixed and strong vaccine, was used instead. The latter was employed in the Durbhanga jail in April, 1896, during the progress of a very fatal epidemic. The prisoners were paraded, and every second man or woman was inoculated. The result was that after the inoculation among a strength of

99 non-inoculated, there were 11 cases (11·11 per cent.) all fatal.

110 inoculated, there were 5 cases (4·55 per cent.) with 3 deaths (2·73 per cent.).

The strong vaccine was used on a large scale on coolies of the Cachar tea gardens who, inoculated and uninoculated, lived together in the same huts. The results are recorded by Dr. ARTHUR POWELL:—

6,549 uninoculated had 198 cases (3·02 per cent.) with 124 deaths (1·89 per cent.).

6,778 inoculated had 27 cases (0·47 per cent.) with 14 deaths (0·24 per cent.).

The two vaccines with which the Indian experiments were made, and which established their protective value, consisted of live cultures. Vaccine II. was a strong vaccine fixed in strength by a process in the laboratory, into which I need not enter, but which is frequently erroneously called KOLLE'S method by those who are not familiar with

the fundamental experiments made by HAFKINE in India. Vaccine I. was an attenuated preparation of Vaccine II.

Experience with the inoculations indicated that the weak vaccine was not so protective as the strong, and that the strong vaccine, though it caused, when inoculated into a guinea pig, without a preliminary inoculation of the weak vaccine, a necrotic swelling produced no such effect on man. In fact the experiments on man brushed aside many of the theories and deductions formed from similar experiments on laboratory animals. Another experience was that it is not safe to rely on the vaccine giving protection for more than fourteen months, and lastly, that though the protective effect of the weak and strong vaccine protected against attacks of cholera, they had not the same protective effect against death as the two strong vaccines when an inoculated person was attacked with the disease. It was because of the experience gained with the cholera vaccine that a different mode of preparation of the vaccine against plague was adopted, and because plague is a septicæmic disease, it was devitalised. The value of the chemical product thus prepared and used as a prophylactic for plague, both in protecting against attacks of plague and reducing the chances of death when attacked, have been well-established. In cholera, some devitalised preparations of vaccines were used in India, but no opportunity was offered for testing their efficiency. It was the live cultures that were used, and it is generally agreed that they are more efficient than dead cultures. HAFKINE holds the view that similar experiments are needed to test the value of the devitalised vaccines of cholera, as those which were employed to ascertain the efficacy of the live vaccines of cholera, and the devitalised vaccine of plague.

There can be no doubt that devitalised vaccines, if efficient, are the best for administration on a large scale, and although there has been no scientific proof of their efficiency, based on researches on man, such as have established the value of the living vaccines of cholera and the devitalised vaccines of plague and typhoid fever, yet there are occasions on which they have been used in which evidence of a general character has indicated that they also are of great value and similar in character to those of typhoid and plague. When visiting KITASATO's laboratory in Japan, in 1902, I found the devitalised cultures of Vaccine II. were being used with what was believed to be satisfactory

results. Over 70,000 people were inoculated with this vaccine. CASTELLANI has used the devitalised vaccines in Ceylon since 1905, combined with those of typhoid fever and paratyphoid A. and B. in one mixture.* This is a combination which saves and eliminates an unnecessary number of inoculations and which at the same time does not produce any antagonistic effect. The devitalised preparations were employed in Petrograd in 1908 and 1909 and in Batavia in 1910 and 1911; over 30,000 people being inoculated in each of these towns. Similarly the devitalised preparations were employed on a large scale by the Greeks during their military operations in Macedonia in 1913. The appearance of the first cases of cholera at Chataldja in the Turkish army, and later in the Bulgarian army, decided the Greek authorities to begin a general vaccination of the army and of the civil population of that part of Macedonia occupied by the Greek army. For this purpose two anti-cholera ambulances were attached to each division of the army. One was a rapidly travelling section containing a well-equipped laboratory and disinfecting stove, under the direction of a medical bacteriologist, and the other a stationary section, under the direction of a medical man, equipped with material necessary for the transport and treatment of twenty-five cholera patients. Some fifty bacteriologists were employed, of whom thirty-five were civil and fifteen military, and the inoculations were performed by the regimental medical officers and the civilian doctors in different locations, who were supplied with material and printed instructions. The organisation and administration of the anti-cholera campaign, both in the army and civil population, was placed in the hands of Professor C. SAVAS working in conjunction with M. MANOUSSOS, the principal medical officer of the army. Professor C. SAVAS gives in the *Bulletin of the Office International D'Hygiène Publique*, of October, 1914, a very full account of the measures taken to carry out anti-cholera inoculations in the army and civil population in the infected area, and the effect they had in checking and suppressing the epidemic.

Approximately half a million persons were inoculated. This included about 150,000 soldiers, 350,000 civilians and refugees in Macedonia, and about 150,000 civilians and refugees in Salonika.

In ten divisions, consisting of 114,805 soldiers, which took part in

* *British Medical Journal*, November 7th, 1914.

the Græco-Bulgarian war, there were only 2,192 cases of cholera (19 per 1000).

The incidence on inoculated and not inoculated was as follows :—

Two vaccinations.	91,224 soldiers had	644 cases =	7 per 1,000.
One vaccination	14,613	„ 618 „ =	42 „
Not vaccinated	8,968	„ 834 „ =	93 „

Those vaccinated only once had six times more cholera cases than those vaccinated twice, and those not vaccinated had fourteen times more. If to the non-vaccinated be added ninety-six fulminating cases which are stated to have occurred among them, the ratio rises to 103 per 1,000.

It was reported by the principal medical officers of divisions that as soon as the vaccination of these were finished, cholera disappeared as by enchantment, and only remained sporadic among soldiers sent to fill up vacancies, and who had not been vaccinated, and this though the soldiers remained in localities where cholera was prevailing amongst the civil population and the refugees.

Further, in the first division, specially in which the first cases of cholera occurred, and in which the double vaccination had been completed before hostilities commenced, there were only a few cases of cholera reported, and only among soldiers who had been sent from Athens and had not been vaccinated, whilst the other divisions which co-operated with them, were attacked by the epidemic.

It was noticed also that in the towns and villages a double vaccination of the inhabitants was followed by a sudden decrease and prompt disappearance of the epidemic, and it is to these vaccinations that Professor SAVAS ascribes the control and suppression of the disease, both in the army and among the civil population of the infected towns, and the protection of Greece from the ravages of cholera when the population was under conditions where other sanitary precautions were difficult, or impossible to adopt.

The success attending these inoculations is similar to that which I have had in regard to plague. In 1913 the whole population of Mombasa, resident and floating, was inoculated during an epidemic of plague, with the result that the disease was effectually stamped out. I had a similar experience in 1908 in West Africa. In both localities pneumonic, as well as bubonic, plague prevailed. The inoculations were,

of course, combined with all other known methods of combating the disease.

Professor SAVAS attributes to the inoculations the saving of Greece from a serious epidemic ; concludes that 99 per cent. of persons inoculated twice remained refractory to the epidemic ; and classes anti-cholera inoculations among the most efficacious preventatives against cholera.

While recognising the extraordinary good effect which the inoculations had in checking and suppressing cholera in this particular campaign, there is one important point which has to be remembered in order to gauge the power of the inoculations at their true value, and that is that the type of cholera was not of a virulent character except in the ninety-six fulminating cases among the non-inoculated. The vaccines were capable of dealing with the epidemic, but it was a comparatively mild epidemic that was dealt with.

There is much variancy in the virulence of epidemics of cholera. I have seen an epidemic in which the mortality was as high as between 80 and 90 per cent., and I have seen others which have had a mortality of less than 20 per cent. It is important in preparing vaccines against an epidemic to obtain for the inoculations a natural strain of cholera bacillus from as virulent a type of cholera as possible, in order that the immunising effect shall be well above the type of the epidemic, and in order that it can be maintained with ease at a high and fixed state of virulence in the laboratory. Whether the present Russian strain will be the most effective to combat any natural exaltation of epidemics due to recrudescences or importation under the conditions mentioned, may well be a matter of doubt, seeing that since 1911 its virulence and capacity to spread have been diminishing.

I think CASTELLANI's method of mixing the vaccine is well worth consideration, as being practical and convenient. It is not doing anything different from inoculating on one arm with typhoid vaccine and vaccinating on the other at the same time against small pox.

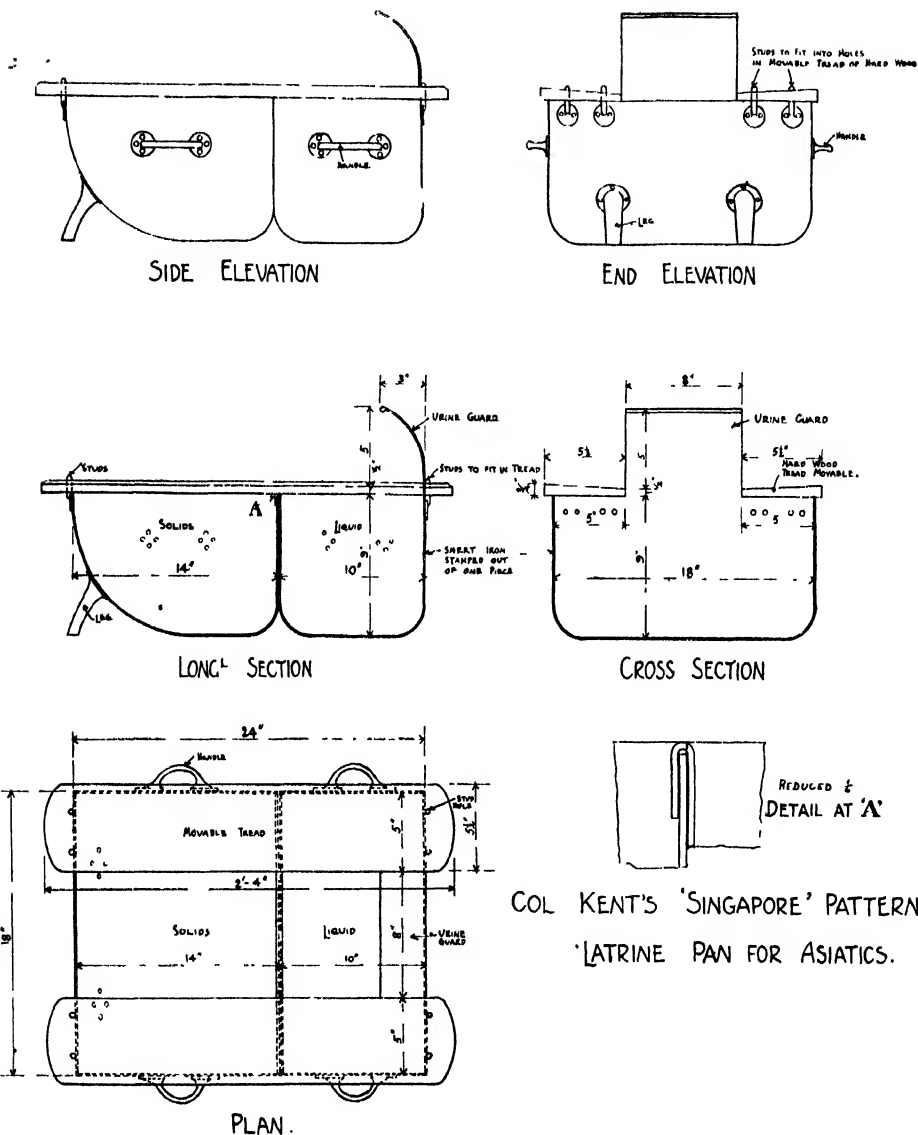
This is not a paper dealing with the treatment of cholera, but before closing I should like to record my opinion that LEONARD ROGERS's method is a valuable addition to the physician's resources when called upon to treat the disease.

The PRESIDENT: I think that this discourse of Professor SIMPSON's to-night has been very apropos on account of the condition of affairs in Europe. Professor SIMPSON's address has brought back to me a great number of memories. In 1894 I was at the Indian Medical Congress when, as he says, he read a paper there. At the same meeting was Dr. ERNEST HART. He came to teach India. He said, quite rightly, you could only eat cholera, or drink cholera, and spoke as if service men in India knew nothing. There were a considerable number in India who had in practice carried out these ideas. They considered that Dr. HART was teaching his grandmother.

With regard to the water borne theory with respect to cholera, I had a striking lesson on the subject. Before I went to Calcutta I was at a certain Station, and in the hospital were some very bad cases of cholera. One of these, at night, escaped from the vigilance of the nurses. There was a very fine well in the compound, from which all the menials derived their water supply. The cholera stricken individual got into that well and spent the night there. He was taken out in the morning alive, and was carried to the Ward. There had been no cholera amongst the subordinate staff. About 24 to 36 hours later there was a virulent outbreak amongst those whose custom it was to use the well water. The well was cleared and disinfected. The outbreak subsided. An example like that, of course, brings the lesson home to one very strongly. That occurred long before Dr. HART came to India.

Professor SIMPSON has not said anything whatever about treatment, except in the last paragraph of his paper. There are certain questions I put to him. First: When, in his opinion, are cholera cases bacilli free? Secondly: In his carrier cases, how is he going to eradicate the vibrios from the gall bladder? Thirdly: regarding vaccination, certain authorities state that you lessen immunity to cholera during the first two days after vaccination. What is Professor SIMPSON's opinion?

The War and Cholera—These are two points which naturally strike anyone having charge of troops. First, the factors in producing an epidemic; and secondly, the best way to exercise prophylaxis against it. Amongst the factors, it has been put very well that there are five "C's." The *carriers*, two kinds, chronic and healthy. The *climate*, which undoubtedly influences the spread of cholera, because we know that cholera, though introduced frequently into Europe and America, does



not spread as it does in tropical climates. The *crowds* that Professor SIMPSON spoke of, whether pilgrims, fairs or armies. *Contamination of food or drink*; and *conservancy*—the sins of conservancy.

The next important point is prophylaxis, for the best way to escape death from cholera is not to get it. Professor SIMPSON and I have been through a number of cholera epidemics, and I must say at times it somewhat shatters the nerves, but the point I have always gone on personally, first of all, is to prevent the entry of the bacilli into the body. Drink boiled water, eat hot food. Keep your eating utensils clean, observe the strictest personal cleanliness for the hands, never put them to the mouth. Next, increase the resistance of the body. That is important during an epidemic. Do not go and see cases with an empty stomach. Avoid any tendency to indigestion or diarrhœa. If there is a tendency to it, be content with food of a more simple nature. A most excellent thing to take, I have found, was diluted hydrochloric acid, 20 to 30 drops, three times a day. The third point in prophylaxis is isolate your patients and contacts, carriers and infected objects, and lastly attend to the night soil. There is one point as to night soil. Colonel KENT, R.E., of the War Office, has devised a most excellent form of night soil stool. It is for natives of India. We all know it is much more easy to destroy fæces if the urine is not mixed with it. There are two receptacles, the front one is for the urine and the back for the fæcal matter. The best way of treating fæcal matter is by the systematic use of chlorinated lime or cressol. Boil the urine.

Professor SIMPSON spoke very truly with regard to the relative virulence of epidemics, and in comparing mortality statistics and methods of treatment—do not forget it. Another point is the dose of poison that gets into you. There are few epidemics in which you do not get a little. You eat the small dose, the large dose eats you.

Some time ago I suggested we should have a paper in this Society on differences of opinion on tropical diseases—a resumé of the year's work. Now two points have come up to-night. One of these is with regard to the effect of the bile or the cholera vibrio. Researches reported lately state that the bile is a natural protection against cholera. We have Major GREIG shewing and demonstrating that in the gall bladder the vibrio rests in safety. It lives secluded there; it is in a position not to be attacked by anything, and in a suitable medium for growth.

The other point is with regard to vaccination, whether it lessens immunity.

I am very glad indeed that Professor SIMPSON alluded to Major GREIG'S researches. They are of the greatest interest and value, and determine the scientific explanation of the mechanism of the production of carriers. The manner in which the cholera vibrios pass from the intestinal channel to the liver and biliary ducts; also GREIG has well brought out the importance of carriers, demonstrating them as the starters of sporadic cases as well as the possible cause of epidemics, and pointing out that the discharge of the vibrios from the gall bladder is intermittent and not regular.

It was a pleasure to me, personally, to be reminded of former days by Professor SIMPSON to-night, because I think we have both gone through the same time, epidemics of small-pox, plague and cholera. Calcutta is a wonderful city.

Surgeon-General Sir DAVID BRUCE: I have never quite understood why anti-cholera vaccination has not become more popular in India. We do not seem to hear much about it of late years. Is it because it is thought to be a failure? Perhaps Professor SIMPSON will give us some idea as to this.

I think HAFFKINE deserves great credit for having worked out anti-cholera vaccination.

Sir RONALD ROSS: I think I can explain one reason why HAFFKINE'S anti-cholera vaccination has not been employed and heard of so much now. There is another method of preventing cholera, which is known as HANKIN'S method. I had to deal with several outbreaks of cholera in Bangalore in 1896, nearly twenty years ago, and I preferred the HANKIN method to the HAFFKINE method, simply because it was impossible to inoculate a population of 100,000 in a few weeks. I understand there is a proper place for each method. For the natives in India one prefers HANKIN'S method, but in the army in Greece, one prefers HAFFKINE'S method. Each method is applicable in the appropriate case.

Fleet-Surgeon P. W. BASSETT-SMITH: There is just one point I

should like to refer to. Professor SIMPSON spoke about cases occurring on board ship. That, of course, is a point of very great importance to us from a practical point of view. During the summer-time there may be a great deal of movement of troops, and troop-ships will be carrying possibly infected cases. Bearing that in mind, it becomes us to remember the great value of HAFKINE or KOLLE preparation for producing immunity, and whether it would not be advisable to recommend that those permanently employed on those hospital ships who had to attend on the sick should receive a protective inoculation. Its use might be made compulsory on those ships in the Mediterranean stations. The work is made much more important because one now recognises that the disease is septicæmic in character, so that we have greater reasons for these important methods that should be taken to protect the individual from possible danger from those he may associate with in the form of carriers.

Professor W. J. SIMPSON: I thoroughly appreciate and reciprocate, Mr. President, your kind remarks about our association in Calcutta, bringing back very pleasant memories to both of us.

With regard to the question of how long the bacillus remains in the convalescent: well, that is a difficult matter to say. As a rule, it is about three weeks, but it is not safe to send out a cholera patient without examining the stools at least twice, to ascertain if there are any bacilli, because it has been found that that is the only way of coping with the carriers. There will be a certain percentage of cases in which the bacilli continue for many days—even for fifty-five days—and they have been found after a year. How much longer has not been ascertained.

Then the question was asked how the bacilli could be eradicated from the gall bladder. I am afraid that is a puzzle. It is one of those matters for scientific research. It is not an easy matter to get to the gall bladder, as one knows with regard to typhoid fever, and I know of no medicine at the present time that is able to deal with that. Major GREIG hopes one day to hit upon something to remove the bacilli from the gall bladder, but I am afraid there is nothing in his valuable experiments so far which encourages the hope of a satisfactory solution of the problem.

Then there was another question as to the lowering of immunity

during the first two days. In all the experiments that were made on man, this immunity was not lowered. The experiments on animals indicate there is a lowering of immunity in them, but the fact that in man there is a reduction during the first four days amongst the inoculated, both in mortality and in attacks, when compared with the not inoculated, seems to indicate there is no lowering of immunity at all, but on the contrary a gradual and general rise in immunity up to the fourth day, and after that, this immunity is complete. I know that CALMETTE brushed aside many of the theories and deductions formed from similar experiments on laboratory animals, and others have indicated that there was a lowering of immunity in their experiments on animals, but it was not so in the experiments in India, as I have already stated.

The PRESIDENT: In the Bulgarian war in 1913 it was shewn that it predisposed them to attack for two days after inoculation. The succeeding eight to ten days full protection was obtained. After the second dose there was again loss of immunity followed by full protection.

Professor SIMPSON: I should like to see these experiments carried out in time of peace. In time of war one can only get facts with reference to the larger questions as to whether inoculations give immunity rather than any of these refinements. The Indian experiments were carried out during a time of peace, under specially favourable conditions, with every precaution, supervision, collection, weighing, and verification of facts, which would be quite impossible during a time of war. We inoculated in houses where there were actually cases, and we found that a number of them took cholera, it is true, but it was well within the period of incubation. I take it that this apparent lowering of immunity for two days in the Bulgarian Army is more likely to be explained by those who were inoculated being in the stage of incubating the disease. However, the matter is very interesting, but from our experiments, and from those that have been carried on in times of peace, nothing like that stated as occurring in the Bulgarian Army has been noticed.

I hope I did not convey the idea that the cholera bacillus was not isolated and cultivated in the epidemics in Europe. Immediately after KOCH discovered the bacillus in Egypt in 1883, and cholera occurred in

Europe in 1884, many of the cases were examined for the cholera bacillus, in fact Dr. SHAKESPEARE has written a large book on the subject of cholera in Europe in 1884, and he mentions that in most countries the bacillus was found in cases of cholera, although at the time many scientists were doubtful as to what relation it had to cholera. It was in India where this controversy was keenest and continued for years. KLEIN came to India, and I think his researches rather tended to mislead people at that time.

Cholera inoculations were not given over in India because they were considered to be a failure. It was because plague came on the scene, and everybody was interested in plague, and inoculations against cholera went into the background altogether, but even then inoculations were continued among coolies going to Assam for about ten years with very good effect; the reason for them ultimately being stopped I do not know. It is very likely that the medical men who were interested in the cholera inoculation, such as Colonel VAUGHAN and others, were moved to some other station and the inoculations were dropped. However, I think it was mainly due to plague coming on the scene and absorbing attention.

I think that Fleet-Surgeon BASSETT-SMITH's suggestion is a good one, with regard to hospital attendants, who certainly ought to be inoculated if there is any cholera, or likely to be any cholera patients come into the hospital. I can recommend inoculation. I have been inoculated against many diseases, and many times. I have been inoculated several times for cholera, and those who have been inoculated against typhoid will know that it is not a very serious operation.

I beg to thank you for the very kind way in which you have received my paper.

TRANSACTIONS
OF THE
SOCIETY OF TROPICAL MEDICINE
AND HYGIENE.

APRIL, 1915.

VOLUME VIII. No. 6.

Proceedings of a Meeting of the Society on Friday, March 19th, 1915,

PROFESSOR W. J. SIMPSON, C.M.G., M.D., in the Chair.

SOME INTERESTING DRUGS OF TROPICAL ORIGIN.

BY

FRANK LEE PYMAN, D.Sc., Ph.D.

(Director of the Wellcome Chemical Research Laboratories).

The title of this paper is somewhat vague and calls for further definition, for the many drugs of tropical origin can be discussed from several points of view. My object, this evening, is to remind you of some of the drugs which we obtain from the tropics, and to give you a short account of the history and natural philosophy of a few of the substances employed in medicine, especially in tropical medicine. Also, I have not scrupled, in one or two cases, to bring within the scope of this paper drugs which are of interest in tropical medicine, even when they can hardly be described as of tropical origin. Only a few drugs can be dealt with in the course of a short paper, and the selection of these has been more or less capricious, but governed to some extent by the desire to utilise the material rendered available by researches

conducted in the laboratories now incorporated in the Wellcome Bureau of Scientific Research.

It is desirable to have some plan of connecting the diverse drugs which we shall discuss, and I think it will be well to treat them geographically. We will follow the sun round the tropical belt of the world, commenting on some of the drugs indigenous to the different countries we shall visit.

IPECACUANHA.

Starting from this country we first reach Brazil, which leads us naturally to the subject of ipecacuanha. Ipecacuanha root is stated in the B.P., 1914, to be derived from *Psychotria emetica*, STOKES. This plant, for which other authorities prefer the name *Cephaelis ipecacuanha*, belongs to the family *Rubiaceae*. It is indigenous to Brazil, but is also cultivated in the Straits Settlements.

The ipecacuanha plant is a low, soft-wooded shrub, growing in the rich soil and the shade of forests lying along the banks of the rivers. It flourishes best where the rainfall is abundant, but where the rivers do not overflow. An interesting account of the method of collection has been given by WEDDELL, in 1849. The native collector (*poayero*) pulls the stems of a clump with one hand, whilst loosening the roots with a pointed stick in the other. After the whole mass has been dragged up, the roots are freed from earth by shaking, and dried. Small fragments of the roots remaining in the ground soon give rise to fresh plants, so that extirpation does not take place.

The emetic properties of the root were known to the Brazilian Indians, who had a fable to the effect that the dogs of the forest used to chew the root after drinking too freely of foul water, when they forthwith vomited and became well. The Portuguese, who occupied the country later on, called ipecacuanha "rais d'oro," or golden root, on account of its virtues.

The first published record of the plant occurs in *His Pilgrimes*, a treatise published in London by SAMUEL PURCHAS in 1625, where the following passage occurs:—

"*Igpecaya* or *pigaya* is profitable for the bloudie flux. The stalke is a quarter long and the roots of another or more, it hath only four or five leaves, it smelleth much wheresoever it is, but the smell is strong and terrible."

In 1648, PISO and MARCGRAF published their *Historia Naturalis Brasiliæ*, in which an accurate description of the plant is given. The root was first brought to Europe by LE GRAS, in 1672, and appears to have been exploited chiefly by a certain physician, J. A. HELVETIUS, in Paris. At first, treatment with the new remedy was unsuccessful, since the drug was apparently administered in too large quantities. Later, however, HELVETIUS prescribed the root with success in cases of dysentery, and advertised the fact on placards affixed to the corners of the streets, but did not make public the origin of his remedy. The fame of HELVETIUS' results attracted attention in high quarters, and eventually the drug was tested in the Paris Municipal Hospital. After many important personages, including the Dauphin, had benefitted from it, King Louis XIV. bought the secret of the root for 1,000 louis-d'or, and made it public in 1688. Since that time ipecacuanha has been generally recognised as an important remedy for dysentery, but has fallen out of favour several times compared with other modes of treatment. A notable revival of its use took place in 1858, when DOCKER prescribed large doses in dysentery with success, but subsequently other treatments were preferred, and it was reintroduced by Sir PATRICK MANSON about 1902.

An important date in the history of ipecacuanha is 1817, when PELLETIER and MAGENDIE isolated from the root a principle which they termed emetine. This was obtained in a yield of 16 per cent., and must, therefore, have contained much non-alkaloidal material, for the root does not contain more than 3 per cent. of total alkaloids. As the result of their chemical and physiological investigation they came to the following conclusion:—

“Emetine may be substituted for ipecacuanha in all cases where we employ this medicine, and with the more advantage as this substance in a determined dose has always constant properties, which is not the case with the different species of ipecacuanha that are met with in commerce, and it has also the further advantage of having very little taste, and scarcely any odour.”

Later on PELLETIER obtained a pure alkaloidal principle in a yield of about 1 per cent. The first reference to the use of the alkaloid in

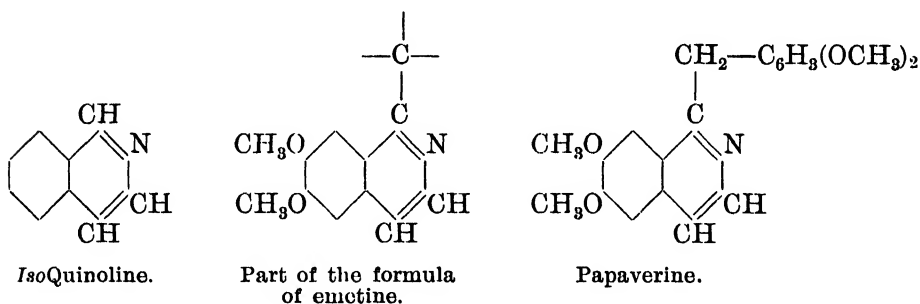
medicine is in June, 1829, when BARDSLEY, of Manchester Infirmary, recorded the following observation :—

“In some cases of dysentery, chronic diarrhœa, and chronic pulmonary catarrh, I have derived from emetine in combination with a small proportion of opium, much benefit.”

Again, in 1890, TULL WALSH administered it in dysentery with marked success. In 1894, however, the chemists, PAUL and COWNLEY, published the first of an important series of papers in which they shewed that the alkaloid then known as emetine was not a homogeneous substance, but consisted of a mixture of alkaloids, which they shewed how to separate. The amorphous, ether-soluble alkaloids were separated into two different bases, called emetine and cephæline, both of which form crystalline salts. Up to the date of PAUL and COWNLEY's work, therefore, observations made with emetine referred to the mixed alkaloids, containing the more toxic base cephæline.

The pharmacology of the pure alkaloids was first studied in 1895, by WILD, who found that both emetine and cephæline possessed emetic properties, but that the latter was quantitatively about twice as powerful as the former in this respect. Other actions of the pure alkaloids were studied, and the separate use of the pure substances was advocated. In 1910, VEDDER demonstrated experimentally the high amœbacidal action of emetine, and suggested the application of his results to pathogenic human amœbiasis. In 1912, ROGERS found that *Entamœba histolytica* in dysenteric stools was killed immediately by a 1 in 10,000 solution of emetine hydrochloride, and apparently killed after a few minutes by as weak a solution as 1 in 100,000. His results led to his now well-known method of treatment of amœbic dysentery by hypodermic injections of soluble emetine salts. I have noticed in the literature a suggestion based on PELLETIER and MAGENDIE's statement that the substitution of emetine for ippecacuanha may be regarded as a revival, and historians, leading up to ROGERS' work, have drawn attention to the previous results of BARDSLEY and TULL WALSH with emetine in dysentery. I would, therefore, like to point out that the pure alkaloid, emetine, was not discovered until 1894, and that to ROGERS is due the credit, not only for his hypodermic method of applying the drug, but also for the use of the salts of the pure alkaloid, in dysentery. The observations of VEDDER and ROGERS that emetine kills amœbæ have

placed the use of ipecacuanha on a scientific basis, and have shewn that pure emetine is the important constituent of the drug. Protozoological and clinical experiments by ROGERS shewed that pure emetine was more efficacious than the mixed alkaloids of ipecacuanha, and that these, in their turn, were more efficacious than cephaeline. At this point it may be interesting to recall that the use of ipecacuanha-*sine-emetina* has been advocated from time to time, but now that the mode of action of ipecacuanha in amoebic dysentery is understood, the use of the de-emetinised product in this disease is not likely to be repeated. The chemistry of the alkaloids of ipecacuanha has been studied at length by many investigators, but it was only in 1914 that it was first shewn that emetine has the formula $C_{29}H_{40}O_4N_2$, and is the methyl ether of cephaeline $C_{28}H_{38}O_4N_2$, from which it can be prepared. It was also shewn that these alkaloids are derived from *isoquinoline*, the parent compound of the alkaloids of opium, and a part of the skeleton formula of emetine was deduced.



This part is common to papaverine, and some of the other alkaloids of opium, a fact which is of interest in the following connection.

R. MARKHAM CARTER has stated (*Ind. Med. Gaz.*, 1914, 49, 109) :—

“The true emetine amoebicidal effect is delayed in patients who are confirmed opium-eaters, and experience has shewn us that in spite of vigorous emetine treatment, it is from the slaves of opium that we get our cases of rapidly fatal, acute, gangrenous dysentery. I believe this is due not to an antagonistic neutralisation of the action of emetine by one of the many opium alkaloids, but to the effect of opium on the intestinal contents, whereby the amoeba-laden faeces stagnate in the pouches of the large intestine.”

It occurs to me that there is another possible explanation of the idiosyncrasy of opium-eaters to the drug, and this is suggested by the paragraph immediately following that just quoted :—

“In the treatment of human amœbiasis, the doses of emetine for an adult should be at least 1gr. per diem, and in severe cases the drug should be pushed without hesitation. Minute doses of $\frac{1}{4}$ gr. do harm instead of good, as I believe they so sensitize the residual store of undestroyed amœbæ in the gut-wall as to render them emetine-proof.”

The suggestion here is that the amœbæ develop a tolerance to emetine when treated with small quantities, and in view of the partial similarity of configuration of some of the alkaloids of ipecacuanha and opium noted above, it may well be that, in the case of opium-eaters, the amœbæ have developed a tolerance to certain “pharmacophore” groups common to emetine and some of the opium alkaloids.

CINCHONA.

From Brazil we pass across to the west of South America, and meet with cinchona, the “Peruvian Bark.” The *Cinchonas* are indigenous to Peru and some of the neighbouring countries, growing on the eastern slopes of the mountain ranges. The history of cinchona bark is long, interesting and romantic; but it must suffice here to recall that the fame of the bark was first spread abroad owing to the cure of the fourth Countess of Chinchon of a tertian fever, in 1638. The bark was sent to her by the Corregidor Cañizares, to whom its secret had been revealed two years previously by an Indian of Malacostas, and was administered by her physician, Don Juan de Vega. When the Countess returned to Spain, in 1640, she brought back a supply of the powdered bark, and treated with it the peasants on her husband's estates at Chinchon, near Madrid. This led to the name “Countess's powder” for the drug. Later on the bark was distributed chiefly by the Jesuits, and was consequently called “Jesuits' bark.” It was adopted by the London Pharmacopœia in 1677, and the alkaloid, quinine, was isolated from it by PELLETIER and CAVENTOU in 1820.

Since then many different preparations of the alkaloids present in cinchona have been employed in malaria, some of which are crystalline, and others amorphous. The total alkaloid obtained from the bark is

a complicated mixture, varying according to the kind of bark employed. When the bark of *Cinchona succirubra*, PAVON, is used, an amorphous mixture of alkaloids, containing only a small proportion of quinine, is obtained; this is known as "cinchona febrifuge." For the preparation of quinine, other species of *Cinchona* are employed, and the total alkaloid is neutralised with sulphuric acid, when most of the quinine present crystallises as sulphate. The mother liquor from this contains the residual alkaloids, in the form of sulphates, and gives a precipitate of these bases on the addition of alkali. The mixture so obtained is known as "residual alkaloid." This is also an amorphous mixture of bases, but has a composition different from that of "cinchona febrifuge."

	"Cinchona febrifuge."	"Residual alkaloid,"
Quinine	7 per cent.	3 per cent.
Cinchonidine	6 ,,	2 ,,
Quinidine	23 ,,	20 ,,
Cinchonine	19 ,,	35 ,,
"Quinoidine"	29 ,,	30 ,,
Water, etc.	16 ,,	10 ,,
	<hr/>	<hr/>
	100 per cent.	100 per cent.
	<hr/>	<hr/>

Both these amorphous preparations can be separated further into crystalline and amorphous fractions. By suitable treatment quantities of the crystallisable alkaloids quinidine, cinchonine, cinchonidine, and more quinine can be removed from them, and there remains finally an amorphous base from which no more of these alkaloids can be extracted, though it doubtless still contains small quantities of each of them. The final residue is called "quinoidine." This short account will shew, briefly, the relations between the four pure alkaloids—quinine, quinidine, cinchonine, and cinchonidine—which are usually employed in the forms of their crystalline salts, and the three varieties of amorphous alkaloids, "cinchona febrifuge," "residual alkaloid," and "quinoidine." All these preparations have been employed in malaria, and opinions have differed from time to time as to their relative value.

The Madras Commission, in 1866, reported as the result of prolonged clinical trials that the sulphates of quinine and quinidine possessed equal febrifugal power, whilst cinchonidine sulphate was only slightly

less efficacious, but that cinchonine sulphate was considerably inferior to the other alkaloids, although it was a valuable remedial agent in fever.

The results of the *Cinchona* Derivatives Enquiry recently conducted by MACGILCHRIST, however, suggest that cinchonine may be not inferior but superior to the other crystalline alkaloids. He has made a chemotherapeutical study of the four alkaloids with the view of determining which would be most useful for the treatment of malaria. The idea was to determine the relative toxicity to host and parasite in each case, and for the purpose of his experiments the minimum lethal dose for guinea pigs was determined in one case, and the minimum concentration of solution necessary to kill different species of infusoria in the other. The results may be roughly summarized by the statement that, under the conditions of his experiments, if quinine sulphate has a value of 100, then quinidine sulphate has a value of 76, cinchonine sulphate 113, and cinchonidine sulphate 91. MACGILCHRIST suggests, as a result of his work, that cinchonine should be given a thorough clinical trial. He also adduces evidence in its favour from the experience of missionaries that "residual alkaloid" is a better therapeutic agent than "*cinchona* febrifuge" in malaria, pointing out that the chief difference between the two lies in the much larger proportions of cinchonine in the former. This argument certainly appears to indicate the value of cinchonine, but loses point in view of WATERS' recent results shewing that "quinoidine" (which contains no removable cinchonine) is even more effective.

In comparing the two classes, (a) the four crystalline alkaloids, quinine, quinidine, cinchonine, and cinchonidine, and (b) the three amorphous preparations, "*cinchona* febrifuge," "residual alkaloid," and "quinoidine," three chief differences may be noted:—

1. The former are employed as salts, whilst the latter are used as bases. It is possible that the use of the latter as bases may be responsible for the accompanying nausea; and it would be interesting to learn whether the salts of the three amorphous alkaloidal preparations were also liable to cause this effect.

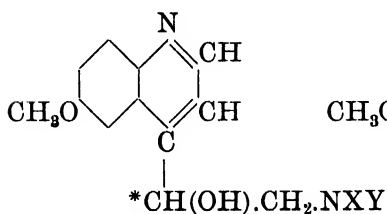
2. The former are crystalline, the latter amorphous. This may well affect the rate of absorption.

3. The former are simple substances, whilst the latter are mixtures.

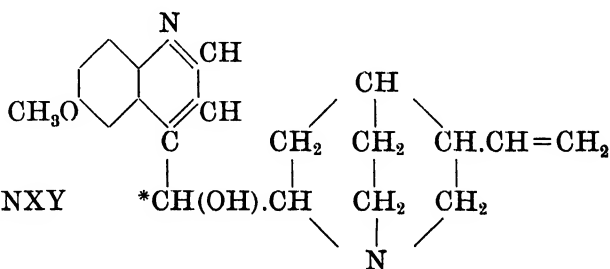
In this connection it is worth while to recall the recent work of STRAUB on the synergism of the opium alkaloids. Starting out from the known difference in therapeutic action between a solution of morphine and laudanum of the same morphine content, he investigated the effect of giving morphine mixed with quantities of the other opium alkaloids. He found that narcotine had a synergetic effect on the action of morphine. Thus morphine when mixed with narcotine in certain proportions was more active than when pure, although the action of narcotine alone is much slighter than that of morphine.

It seems possible, therefore, that the activity of the mixed alkaloids may be influenced by the synergetic effect of its constituents, and it would be interesting to hear of experiments similarly carried out with a mixture of the four crystalline sulphates.

The pharmacology of the cinchona alkaloids has also been discussed by MACGILCHRIST, and he clearly adheres to the view that the typical action of quinine is due to the quinuclidine residue, regarding the quinoline portion of the molecule as undesirable, and responsible for the unpleasant by-effects of quinine. The recent work of KAUFMANN, however, appears to render this position untenable, for the latter author has synthesised a number of quinoline derivatives of the type given below,



Kaufmann's Compounds.



and finds that, in general, they are distinguished as powerful febrifuges, combining a low toxicity to man, with a high toxicity to infusoria and paramoecia. The typical action of the cinchona alkaloids, therefore, appears to be due to the association of the quinoline complex with the ethanolamine grouping .CH(OH).CH₂.NXY. KAUFMANN's compounds contain an asymmetric carbon atom, marked in the formula given above with an asterisk, and he has announced his intention of resolving them

into their enantiomorphous forms. It will be interesting to hear how these compare with each other in efficiency, for they will differ in the same way as quinine differs from quinidine, namely, in the spatial arrangement of the atoms round the asterisked carbon atom.

COCA.

Another important drug-plant indigenous to Peru and the neighbouring countries is *Erythroxylon coca*, LAM., the source of cocaine. This plant is a shrub which attains the height of 6, 8, or even 12 feet when growing wild. It is largely cultivated in the mountainous districts of Peru and Bolivia in plantations known as "cocales," and in these it is not allowed to grow to its full height, for the collection of the leaves would then be inconvenient. The leaves are picked three times a year, about March, June, and November, and are then dried in the sun. The transportation of the product to the coast is a matter of considerable difficulty, as the packages have to be carried on the backs of natives, mules, or llamas.

It is known that the Incas made use of coca leaves in their religious ceremonies; for instance, the sacrificing priest used to chew them when consulting the oracles. Also the Indians from that time down to the present day have chewed the leaves to enable them to withstand wet, cold, or hunger, or to undertake great feats of bodily endurance.

Although the stimulating properties of the leaves have been known to Europeans since the Spanish conquests in South America, the use of cocaine is of recent origin. This alkaloid is stated to have been isolated first by GARDEKE, in 1855, and subsequently, in 1860, by NIEMANN, who gave it its present name. The latter also observed that it produced temporary insensibility on the part of the tongue with which it came into contact. Its properties do not appear to have been studied again until 1884, when a medical student, KOLLER, drew the attention of Dr. BRETTAUER, of Trieste, to its anæsthetic properties, and this physician demonstrated the advantages of the drug at the Ophthalmological Congress in Heidelberg in the same year.

JALAP AND SCAMMONY.

From South America we go to Mexico, where the varieties of *Ipomœa* are indigenous. *Ipomœa purga*, HAYNE, is the source of jalap resin,

and *Ipomœa orizabensis*, LEDANOIS, is one of the plants which furnish the scammony resin now in commerce. The jalap plant is a perennial climber, bearing handsome rose-purple flowers. It belongs to the same family as the *Convolvulus major* of our gardeners. It is a native of the eastern slopes of the Mexican Andes, flourishing at a height of 5,000 to 8,000 feet in places where rain is frequent and abundant. The tubers are dug up at any time of the year, and are dried over the hearths of the Indian huts. The purgative principle is a resinous substance which is easily obtained by extracting the roots with alcohol. We are indebted once more to the Spanish voyagers for the introduction of these drugs, for they noted the use of the tuber of a convolvulaceous plant of Mexico as a purgative, and brought it to Europe during the sixteenth century.

CAMPHOR.

Leaving the continent of America and reaching Eastern Asia, we will first note that the island of Formosa is the chief source of camphor. The camphor industry is carried out in circumstances of great difficulty, for the island is inhabited by savage tribes, who indulge in the habit of head-hunting at the expense of the camphor gatherers. Although these workers are now protected by Japanese soldiers, who have constructed a series of wire defences with forts at intervals, no less than 187 of them were killed, and as many wounded by the savages, during 1912.

Camphor is derived from *Cinnamomum camphora*, FR. NEES et EBERMAIER, and its preparation necessitates the destruction of the tree. This is cut down and chopped into pieces, which are then distilled with water, when the volatile camphor is vaporised and then condensed. There are many references in ancient history to camphor, which was highly valued and brought to kings as tribute; but such references are believed to refer chiefly to Borneo camphor, now known as borneol, which is found in clefts in the wood of *Dryobalanops aromatica*, GARTN., a native of the Malay peninsula.

RHUBARB.

China is the home of rhubarb, which is the powdered rhizome of *Rheum officinale*, BAILL, and other species of *Rheum*, particularly *R. palmatum*, L. *R. officinale* and *R. palmatum* differ to some extent in their chemical constituents, and consequently it is possible to

determine roughly the relative amount of each in commercial rhubarb. In this way it is found that the best samples of the drug consist very largely of *R. palmatum*. *R. officinale* resembles the common garden rhubarb to some extent, but is larger, and differs from it in other particulars. The root is dug up in the autumn, cleaned, cut in pieces and dried. The records of this drug go back further than most, for it was described in a herbal attributed to the Emperor Shen-nung, who reigned about 2700 B.C.

COMBRETUM SUNDIACUM.

We will next visit the Malay Peninsula, and discuss the anti-opium plant, *Combretum sundiaca*, MIQ. This plant is a vigorous, woody climber, abundant on the plains near Kuala Lumpur, in Selangor. It had a considerable vogue in 1906, and the facts concerning it may be worth recalling. The origin of the use of the plant was as follows:—A party of Chinese wood-cutters, working in the jungle, ran short of tea and made a beverage from the roasted leaves of this plant. Eventually they modified the beverage by the addition of opium dross, that is, the residue of opium after being smoked. After drinking this preparation for a week or more in the place of tea, they lost all desire for opium smoking. The news of this cure was spread abroad, and eventually many thousands of people tried it in a modified form. The leaves and stems were allowed to dry, then chopped up and roasted. The roasted product was boiled with water and the infusion strained. Two bottles of equal size were then filled with the liquor, and to one was added a quantity of burnt opium equal to the daily allowance of the patient. Doses of the medicine were given from the bottle containing the burnt opium, and after each dose had been poured out this bottle was filled up again from the second bottle which did not contain opium. The amount of opium taken in each dose, therefore, diminished gradually until a constant amount was reached when the second bottle was emptied. When both bottles were empty the patient should have been cured of all wish to smoke, but if this were not the case, the cure was repeated but with a smaller initial dose of opium.

There is no doubt that a large number of people have been able to break themselves of the habit of opium smoking by this treatment, but such benefit is probably due rather to the gradual

diminution of the intake of opium than to any specific properties of the so-called anti-opium plant.

CHAULMOOGRA OIL.

We now pass on to some of the drugs of India. Chaulmoogra oil is described by the *British Pharmacopœia*, of 1914, as the fatty oil expressed from the seeds of *Taraktogenos kurzii*, KING, and the synonym "gynocardia oil" is applied to the drug. The latter term is a misnomer, and owes its origin to the fact that for a long time the seeds from which the oil is expressed were believed to be the product of *Gynocardia odorata*, R. BR. In 1901, however, E. M. HOLMES stated, on the authority of Sir DAVID PRAIN, Director of the Botanic Survey of India, that the seeds were not derived from *Gynocardia odorata* but from *Taraktogenos kurzii*, KING, and subsequently POWER and his collaborators shewed that the oil expressed from genuine seeds of *Gynocardia odorata* was entirely different in its characters from chaulmoogra oil. *Taraktogenos kurzii*, KING, also known as *Hydnocarpus kurzii*, WARBURG, and *H. heterophyllus*, KURZ (fam. *Bixaceæ*) is a large tree indigenous to parts of Burmah and Assam. The seeds themselves have long been used by the inhabitants of South Eastern Asia as a remedy for leprosy.

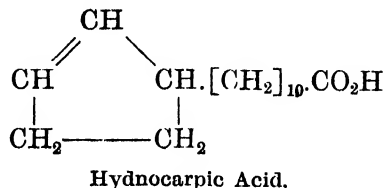
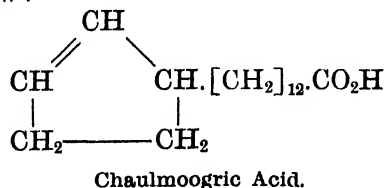
Other species of *Hydnocarpus* yield seeds giving a similar oil. Thus the seeds of *H. anthelmintica*, PIERRE, a plant which is indigenous to Siam, are exported to China as "Ta-fung-tzse." They are also called false, or Chinese chaulmoogra seeds, and have been employed in China, for at least 300 years, in leprosy and other diseases; a preparation of the crushed seeds heated until the mass darkens being applied externally. According to F. PORTER-SMITH, HOBSON reported favourably on the remedy in mild, early cases of leprosy. The same author mentions that some of the chaulmoogra seeds in Chinese shops appear to be derived from *H. venenata*, which have been found almost equally useful in the treatment of leprosy. The seeds of *H. wightiana*, BLUME, a plant which grows in India along the coast ranges from South Concan to Travancore, yield an oil which has long been used by the inhabitants for certain obstinate skin diseases. It has been tried by Europeans as a substitute for chaulmoogra oil, and is stated to have been used in the Bombay Presidency with satisfactory results. Recently, however, E. E. FRANCIS has stated that this oil, whilst of similar composition and appearance to

chaulmoogra oil, has little therapeutic value in leprosy, and its cost in India is only about one-third that of the true oil. There are, therefore, not less than four species of *Hydnocarpus* of which the seeds yield an oil reputed to be of value in leprosy, and it becomes of interest to examine the evidence bearing on their similarity. POWER and his collaborators have carried out a very complete examination of the oils from the seed of the three plants, *Taraktogenos kurzii* (*Hydnocarpus kurzii*), *H. wightiana*, and *H. anthelmintica*, and have shewn them to have very similar physical and chemical properties. They are soft solids, having a more or less faint yellow colour, and a peculiar, rather unpleasant odour. They are characterised by a high degree of optical activity, which is peculiarly striking, since fatty oils in general are either inactive or have a low rotatory power. The melting points and specific gravities (at 25° C.) of the three oils are almost the same, as the following table shews:—

Oil of the Seeds of—

	<i>T. kurzii</i> (Chaulmoogra oil).	<i>H. wightiana</i> .	<i>H. anthelmintica</i> (False chaulmoogra oil).
M.P.	22°—23°	22°—23°	24°—25°
S.G.	0·951	0·958	0·953

The chemical evidence as to the close similarity of the three oils is even more striking. These investigators found that each of these oils consisted principally of the glycerides of two hitherto unknown acids, having the formulæ $C_{18}H_{32}O_2$ and $C_{16}H_{28}O_2$, which they designated chaulmoogric acid and hydnocarpic acid respectively. They were able to shew that these acids contained an unsaturated cyclic complex, and that they were members of a homologous series, having the formulæ given below:—



In physical and chemical respects, therefore, the oils from the seeds of *Taraktogenos kurzii*, *H. wightiana*, and *H. anthelmintica* are nearly identical. The first is chaulmoogra oil, and both the others have a local reputation as a remedy in leprosy. The question whether the two latter

are really inferior to the true chaulmoogra oil, medicinally, is therefore one of some interest.

At this point it may be mentioned that the above authors also made a careful examination of true gynocardia oil, that is the oil expressed from the genuine seeds of *Gynocardia odorata*, R. BR. This oil differed entirely from the oils of *Hydnocarpus* species described above, both physically and chemically. It was a light yellow liquid with an odour similar to that of linseed oil. Its specific gravity was 0.925 at 25°, it was optically inactive, and finally it did not contain chaulmoogric or hydnocarpic acids.

In connection with this account of chaulmoogra and similar oils, it may be noted that "gorli" seeds from Sierra Leone, which are derived from *Oncoba echinata*, OLIVER, another member of the family *Bixaceae*, yield an oil of which the fatty acids consist very largely of chaulmoogric acid.

The oils of *Hydnocarpus* species have more recently attracted considerable attention in Germany. Towards the end of 1910 there were several cases of illness which were eventually traced to the use of a certain brand of margarine. Investigation shewed that the toxicity was due to a plant-fat from Bombay, which formed one of the constituents of the margarine. This fat, which had been imported under the name of "cardamom," or "marotti" oil, was found to consist essentially of the glycerides of chaulmoogric and hydnocarpic acids, and was clearly derived from a species of *Hydnocarpus*, probably *H. wightiana*, whose seeds bear some slight resemblance to Ceylon cardamoms externally. Attempts to "purify" the oil, in order to remove a possible toxic impurity were unsuccessful, for it was found that the toxic ingredients were the glycerides of chaulmoogric and hydnocarpic acids, which formed the main constituents of the oil. Both the oil itself, and the chaulmoogric acid isolated from it, regularly caused vomiting in dogs, due to irritation of the gastric mucosa, and also gave rise, in some cases, to clonic cramp and drowsiness, and in others, to excitement instanced by prolonged barking.

Before leaving the subject of chaulmoogra oil, I should like to refer briefly to "antileprol." Dr. ENGEL BEY, of Cairo, has stated that this was sent to him in response to his request for a purified chaulmoogra oil. "Antileprol" differs from chaulmoogra oil in being a liquid instead of a

semi-solid at the ordinary temperature. Its composition does not appear to have been published, but it probably consists of the purified ethyl esters of the mixed fatty acids of chaulmoogra oil, whereas the natural product contains the acids in the form of glycerides.

GURJUN OIL.

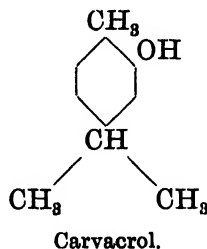
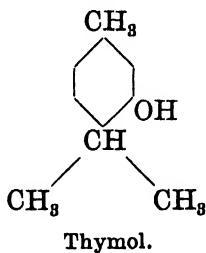
Another Indian remedy, which has been used in the same disease, is gurjun balsam, or wood oil. It is derived from various members of the family Dipterocarpaceæ, of which *Dipterocarpus turbinatus*, GÆRTN. f. (Eastern Bengal), *D. incanus*, ROXB. (Chittagong and Pegu), and *D. alatus*, ROXB. (Chittagong, Burma, Tenasserim and Andamans) are the most important. These are very large trees, forming forests by themselves, and attain a height of 100 to 200 feet. The oil is collected by cutting a notch in the trunk of the tree, close to the ground, and inserting a few red hot coals. These start a flow of juice, which is collected in vessels suitably arranged for the purpose. Every three or four weeks the charred matter is cut off and the cleaned surface charred afresh, the whole operation of tapping continuing for about six months. A single tree sometimes yields as much as 40 gallons of the oil in a season. The oil is commonly used as a water-proof varnish for boats, for painting timber to preserve it from the ravages of insects, and for burning in torches. Its similar action to copaiba was made known in India by O'SHAUGHNESSY, in 1812, but it has never displaced copaiba in gonorrhœa, even in India. As a remedy for leprosy, it was first brought prominently to notice, in 1873, by J. DOUGALL, of the Andamans, who directed that it should be given internally, and also applied externally by the patient himself thoroughly rubbing it over the whole body during two hours a day. Under this treatment improvement was effected, but only of a temporary character. In 1877, A. H. HILSON compared this treatment with the effect of external applications only of Til (*Sesamum*) or sweet oil of the bazaars, and found the latter to be equally efficacious. It therefore appeared that the improvement was due more to the friction with oil than to any specific action on the part of gurjun oil. More recently, however, V. REISNER has remarked on the value of the oil given internally and externally in leprosy.

Chemically, gurjun oil possesses no point of similarity with chaulmoogra oil. The latter is a fixed oil consisting of the glycerides of

fatty acids. Gurjun oil, on the other hand, is a solution of resinous matter in essential oils. It contains 80 to 82 per cent. of essential oil, that is, matter volatile on distillation with steam, 16 to 18 per cent. of neutral resins, and about 3 per cent. of resin acids.

THYMOL AND CARVACROL.

Amongst the medicinal plants of India we may also note *Ptychotis coptica*, D.C., commonly known as *ajowan*. The fruits are the chief commercial source of thymol, yielding about 5 per cent. of a volatile oil, of which approximately one half is thymol. The volatile oils from many other plants also contain thymol; for instance, oil of thyme (*Thymus vulgaris*, LINNE) and the oil of *Origanum hirtum*, LINK. Some other species of *Origanum*, which yield oils of marjoram, contain, in the place of thymol, an isomeric phenol called carvacrol. The two substances differ in constitution only in the position of the hydroxyl group, thymol being a derivative of *meta*-cresol, whereas carvacrol is a derivative of *ortho*-cresol.



Physically, there is an important difference, for whereas thymol is a solid, carvacrol is a liquid at the ordinary temperature.

The extraction of thymol from *ajowan* seeds has hitherto been carried out almost exclusively in Germany, and this has led to a shortage of the drug, in consequence of the war, to such an extent that thymol is now, according to the statement of MOTTER (*Amer. J. Pharm.*, 1915, 87, 35), almost unobtainable in America.

OIL OF CHENOPODIUM.

In view of this position, MOTTER calls attention to the use of oil of chenopodium in hookworm-disease (ankylostomiasis), and a few remarks on this drug may therefore be of interest. The oil, also known as American wormseed oil, is an essential oil distilled from the fruit

of *Chenopodium ambrosioides*, L., var. *anthelminticum*, GRAY, an offensive smelling perennial herb growing abundantly in America, especially in the Eastern United States, as a coarse weed of the roadside and waste places. The bulk of the oil is distilled from plants growing in a section of Carroll County, Md., and is known commercially as "Baltimore" wormseed oil. The oil has a yellow colour, an offensive penetrating odour, and a burning taste. The remedy has an ancient reputation as a vermifuge, and is said to have been used for this purpose in America by the Indians before the arrival of Columbus. The active principle of the oil is a liquid substance, ascaridol, having the empirical formula $C_{10}H_{16}O_2$, of which it contains up to 70 per cent. Ascaridol has the curious property of exploding when distilled under atmospheric pressure, and is decomposed violently by many chemical agents. SCHIMMEL & Co. state that the constitution of ascaridol is probably analogous to that of cineol, the chief constituent of oil of eucalyptus, and NELSON has recently put forward a tentative formula representing it as a terpene peroxide.

The pharmacology and therapeutics of oil of chenopodium and of ascaridol were the subject of several interesting papers by H. BRÜNING, in 1906-1907. He states that the oil, which is used as an anthelmintic in America, has fallen into disuse in Europe, and, as the result of his experiments, praises the oil very highly as an anthelmintic, regarding it as equal, if not superior, to santonin, and recommends its adoption in the German Pharmacopœia. Live ascarides were quickly destroyed in a solution of common salt or Ringer's solution to which the oil had been added, whilst the controls kept well. Even when the oil was applied in a dilution of 1 in 5,000 the ascarides were paralysed within two hours, but they recovered when removed to a non-poisonous liquid. The pure substance, ascaridol, was even more powerful than the oil itself, and is, therefore, the active principle. The toxicity of the oil was tested on several animals, and it was found, for instance, that the toxic dose amounted in the case of guinea pigs, dogs and rabbits, to 0.6, 0.2 and 0.3 c.c. of the oil per kg. body weight respectively. The oil was taken without objection by children, and proved to be absolutely reliable and to cause no secondary symptoms. MOTTER states that, in 1912, SCHÜFFNER and VERVOORT reported on 1,457 cases of hookworm disease treated with oil of

chenopodium over a period of eight months. Favourable results were obtained compared with those given by other vermifuges, and giving eucalyptus oil a co-efficient of 38, beta-naphthol 68, and thymol 83, it was found that oil of chenopodium surpassed them all, with a co-efficient of 91.

SANTONIN.

Before leaving the continent of Asia, I should like to refer briefly to santonin, although this also is not of tropical origin. This drug is extracted from the flower-heads of *Artemisia maritima*, var. *Stechmanniana*, BESSER—known as Levant wormseed—a low, shrubby, aromatic plant, which grows in large quantities on the vast plains or steppes of the Kirghiz, in the northern part of Turkestan. At one time, the collection of wormseed was unrestricted, and the price consequently became very low, but since 1909 the industry has been controlled by the Russian Government in such a way as to provide a living for the Kirghiz inhabitants of the steppes. The wormseed country is divided into districts, and the rights of buying the produce in each are put up to auction. The purchaser of the rights has to take all the wormseed that is brought to him at a fixed price per pound, so that in this way a remunerative wage is assured to the Kirghiz. He also has to bear the expense of watching over his district, to make sure that his wormseed does not get into other hands, and, the districts being large, such expenses are naturally heavy. It is, therefore, not surprising that the price of santonin has risen very considerably within the last few years. The greater part of the wormseed is not exported, the santonin being extracted at Tschimkent in Turkestan. The factory at this place is the only industrial undertaking in the neighbourhood, and labours under great difficulties. It is 60 versts from the nearest station, from which materials have to be hauled, and the hydrochloric acid used in the process of manufacture has to be brought from Rostov on the Don, some 3,800 kilometres away. In the winter, the factory is almost cut off from communication with the rest of the world.

Wormseed is an old remedy. DIOSCORIDES mentions several varieties of *Absinthium* used for ascarides, amongst them being a species called *santonion*, from its growing in the country of the Santones, in Gaul.

The principle, santonin, was discovered by KAHLER, an apothecary,

and ALMS, a druggist's assistant, almost simultaneously, in 1830. The latter named it, and recommended it to the medical profession, pointing out that it is the anthelmintic principle of wormseed.

When santonin is exposed to sunlight it gradually becomes yellow in colour. After prolonged exposure to the sun, in tropical or sub-tropical regions, a deep yellow substance is obtained, called chromosantonin. This product is stated by BEGG to be of value in sprue, whereas ordinary, fresh, white santonin is valueless for this disease.

GUM ACACIA.

We will now deal with some of the drugs of Africa, starting with those of the Sudan, and in the first place I propose to discuss gum acacia. This substance is official in all the National Pharmacopœias. The *British Pharmacopœia*, of 1914, describes it as a "gummy exudation from the stem and branches of *Acacia senegal*, WILLD., and of other species of *Acacia*, WILLD." Although it possesses little medicinal action, it is largely used as a vehicle for more powerful remedies, and is brought within the scope of this paper since its formation has features of interest. The production of gum is the result of a pathological condition of the tree; it is a reaction to irritation.

Acacia senegal (*Acacia vereke*) is called *hashab* in the Sudan. It forms the scrub bordering on the desert, and is found in large quantity in the Kordofan province of the Sudan. It grows on a sandy, ferruginous soil, so poor that it might almost be classed as barren, but which nevertheless supports fair crops of millet. The trees are tapped in the dry weather from October to April, and after the first rains the trees break out into fresh leaf and the exudation of gum ceases. For gum formation, indeed, it is necessary that the tree should be poorly supplied with moisture during the dry season, for trees which are well supplied with water during this period do not yield gum. The collection of gum from the trees was originally conducted without tapping, only the gum which had forced its way through natural cracks in the bark being collected. About 35 years ago, however, the natives commenced artificial tapping, removing longitudinal strips of bark, two to three feet in length and one to three inches broad. No better method of tapping has since been devised, and it has been found that neither the removal of longer or

shorter strips of bark, nor gashing the trees improves the yield. The gum exudes from the wound and forms a tear which is left on the tree for a time sufficiently long to ensure its solidification, and is then collected. The tears vary very considerably in colour, from almost colourless to a deep brown, and are sorted into different qualities, of which a nearly colourless variety is used in medicine. The yield of gum in the course of the season varies in different localities, but amounts to 150 to 300lbs. per acre in a gum garden. The yield from individual trees is very variable; for instance, EDIE, working under BEAM, found that twenty large trees, which had not previously been tapped, gave from one to fifteen pounds as extreme limits during the season. The mode of gum-formation has been the subject of some interesting research work. GREIG-SMITH, working in Australia with a gum-forming plant, *Acacia penninervis*, suggested that the phenomenon was due to a specific micro-organism. From the twigs of this plant he isolated two kinds of bacteria, and found that the prevalent type, which he called *Bacterium acaciæ*, when grown on artificial media, produced a slime from which gum could be obtained. This view of the bacterial origin of gum has received confirmation from the work of BEAM on *talh* trees (*Acacia seyal*), and EDIE on *hashab* trees, in the Sudan. The latter author succeeded in isolating a non-motile bacterium shewing a characteristic habit of growth and bipolar staining from gum-bearing twigs of *hashab* trees, by sterilising the twigs externally by passing them through a flame, and then making cultures from the sap. Sometimes a pure culture was obtained, whilst at other times sub-cultivation was necessary. When this bacterium was grown for a month at 37° C. on an artificial medium containing 4 per cent. of lævulose, 1 per cent. of glycerine, 0·1 per cent. of asparagin, and 0·1 per cent. of potassium citrate, a product was obtained which, after suitable purification, gave a substance resembling gum in its appearance and properties.

A possible method of infection of the gum-trees with the bacteria is the visit of insects. It has been observed that ants and flies are attracted in large quantities to the freshly exuded sap, and the bacterium has been isolated from the sap mechanically adhering to the legs and wings of insects which had visited the trees. The transmission of this disease of the trees by ants is particularly interesting, since these insects possibly also act as carriers in certain human diseases. For instance, it has been

found experimentally in the Philippines and Panama that they spread the organisms of cholera and bacillary dysentery.

A particularly instructive experiment was carried out with the view of testing the effect of different substances, including antiseptics, on the wound in *hashab* trees. A number of trees of nearly uniform size were each tapped to the same extent, a strip of bark about 30 inches long and $1\frac{1}{2}$ inches wide being removed in each case. A group of six trees remained untreated as a control whilst the remainder, in groups of six, were subjected to the following treatment:—

The wounded surfaces were rubbed with the solution to be tested, immediately after tapping, and also on the two succeeding days, in order thoroughly to impregnate the whole wound with the solution in question.

The gum from each group of six trees was collected at intervals between the 28th December and the 13th April, the total yields from each group being as follows:—

Control trees	571 grams.
Wound treated with:—					
(a)	10 per cent. Formalin	1491	„
(b)	1 „ Mercuric chloride	229	„
(c)	3 „ Hydrochloric acid	1135	„
(d)	5 „ Acetic acid	666	„
(e)	5 „ Potassium carbonate	699	„
(f)	3 „ Cane sugar	603	„

It will be observed that the last three substances do not affect the yield of gum within the necessarily large limits of experimental error. Dilute mercuric chloride, however, greatly diminishes the yield. This observation was subsequently confirmed by a number of comparative experiments on two branches of the same tree, one of which was treated with mercuric chloride whilst the other remained untreated, when a similar result was obtained, the treated branches producing no gum, whilst the control branches gave a quantity. It will be seen that formalin and dilute hydrochloric acid largely increased the yield. This is no doubt due to the irritant action of these substances causing an increased flow of sap to the injured parts, for it has been found that bruising the wound after tapping also causes an increased yield.

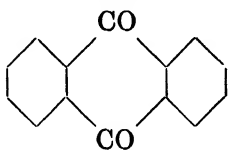
The fact that the powerful antiseptic, formalin, did not inhibit the formation of gum is to be ascribed to its volatility. After evaporation of the formalin, the wound would become reinfected. It is clear from the above experiments that a very strong case has been made out for the bacterial origin of gum, and GREIG-SMITH's view that this phenomenon is the result of a pathological condition is thus confirmed. The causes of gum formation are ably summarized by EDIE as follows:—

“Exudation of gum does not take place from *hashab* trees in those districts where the rainfall is high compared with that met in the gum-producing districts of Kordofan. In the latter case, the tree as a whole is in a state of reduced vitality and the tissues are, therefore, more susceptible to the effects of abnormal injuries. In those districts where the proportion of moisture in the soil is relatively high, the injury produced when the tree is tapped is repaired before the bacteria present have time to produce any appreciable amount of gum. The wounding of the tree through tapping causes a local weakness in the tissues next to the bark, and the cells of the tree are then unable to prevent the rapid increase of, and increased transformation of the sap by, the bacteria. This appears to go on until sufficient new bark has grown over the wound to form a protection for the exposed surface.”

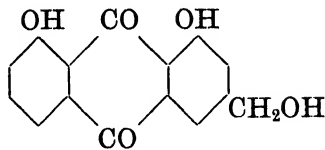
SENNA.

Two more drugs of the Sudan may be mentioned, senna and *Calotropis procera*. Egyptian senna consists of the dried leaflets of *Cassia acutifolia*, DELILE. The shrubs grow wild in the Sudan and the Red Sea littoral of Arabia, and the leaves and fruit are allowed to dry on the branches. The leaflets are collected once a year, in October. Senna is also derived from *Cassia augustifolia*, VAHL, which is cultivated in India, and is regarded by some authorities as botanically identical with *C. acutifolia*. The name, senna, is Arabic, and the drug was first employed by the Arabians, whose writings notice it as early as the ninth century. Senna, in common with several other purgatives, such as aloes, rhubarb, and cascara, owes its activity to derivatives of anthraquinone. Many of these are very complex, whilst

others are of simpler constitution such as aloe-emodin which is believed to have the formula given below.



Anthraquinone.



Aloe-emodin.

Some simple synthetic derivatives of anthraquinone, which is a coal-tar product, have also been tried as purgatives, but do not seem to have been particularly successful.

CALOTROPIS PROCERA.

Calotropis procera, R. BR., is one of those drugs of which preparations were official in the Indian and Colonial Addendum of 1900, but do not figure in the new *British Pharmacopæia*. It is a common weed throughout the Sudan, and is known to the natives as "ushar." The leaves are used in the preparation of "merissa," the native beer, and this use sometimes leads to cases of poisoning. When wounded, all parts of the plant exude an acrid, milky juice, having a nauseating odour. This juice, when applied externally, acts as a powerful irritant, and, when taken internally in large doses, causes vomiting and purging. It has frequently been used for infanticide. Medicinally, *Calotropis procera* has long been used in leprosy and various skin diseases. The plant also grows in India, where it is known as the Arka tree, and is mentioned by the earliest Hindu writers. The leaves have been used in sun-worship and other religious ceremonies.

According to the *Pharmacographia Indica*, a custom general amongst all castes of Hindus is that a man who has lost three wives must make his fourth marriage with the Arka tree, after which he may take a fourth human wife. The object of this procedure seems to be to transfer the man's ill-luck to the plant. *Calotropis procera* was also used by the Arabs, in early times, in rites designed to produce rain. The dried plant was attached to the tails of bulls, and lighted. The animals were then driven from the mountains, and an effect of artificial lightning was produced, from which results in the way of rain were expected.

STROPHANTHUS.

Africa furnishes certain interesting drugs, whose introduction into medicine is due to their use as arrow poisons and ordeal poisons.

Strophanthus kombé, OLIVER, which is indigenous to East Africa, is an example of the first class. It is the source of the famous kombé arrow poison, which is prepared by pounding the seeds to a pulp in a mortar, and adding some sticky plant juice. This mixture is smeared on the shaft of an arrow, which is then capable of killing all except the largest animals. The discovery of the source of the poison was made, in 1861, by Sir JOHN KIRK, who met with great difficulties in his search. The natives were very unwilling to disclose the secret of the kombé poison, and invariably gave him a false plant. At length he saw a plant climbing on a tall tree, but was unable to persuade the natives to pick specimens. When he attempted to collect some himself, however, the natives were afraid he might poison himself, and warned him that this was, in fact, the kombé poison plant.

Physiological experiments carried out by SHARPEY, in 1862-1863, and by HILTON FAGGE and STEVENSON, in 1865, shewed that the seeds contained a cardiac poison. The chemistry and pharmacology were subsequently studied at length by T. R. FRASER, who recommended the adoption of the drug at the British Medical Association Meeting, at Cardiff, in 1885.

PHYSOSTIGMINE.

An example of a drug which has come to our knowledge owing to its use as an ordeal-poison is supplied by *Physostigma venenosum*, BALF. This is a member of the natural order *Leguminosæ*, and belongs to the tribe *Phasoleæ*. It is a perennial plant closely resembling the common scarlet runner, but has a woody stem, often an inch or two thick, and climbs to a height of about 50 feet. It frequents the neighbourhood of streams in the countries adjacent to the Gulf of Guinea. The fruits have been called "the ordeal beans of Old Calabar," or, shortly, Calabar beans, and are named "*eséré*" by the natives. The first account of the use of the beans as an ordeal-poison was given by W. F. DANIELL in 1846. He stated that amongst the negroes, "persons suspected of a crime are forced to swallow a deadly poison made from the poisonous seeds of an aquatic, leguminous plant which rapidly destroys life." The

judgment of the trial by ordeal was as follows: if the suspect vomited the poison, he was not guilty; if it killed him, the crime was proved; and if it caused purging, he was sufficiently guilty to be sold into slavery. About 1860, the plants became very rare, owing to the action of the native king, who had most of them destroyed, and monopolised the remainder in the interests of justice. The plant, which furnished these Calabar beans, was characterised by BALFOUR in 1860, and the alkaloid was isolated three years later by JOBST and HESSE, and called physostigmine. In 1865, VEE and LEVEN succeeded in obtaining it in a crystalline form and called it eserine. The myotic properties of the beans were first recorded in a publication by FRASER in 1862.

CONCLUSION.

We have now completed the circuit of the globe, and it remains to make a few comments of a general nature. Individual drugs have been adopted by physicians at all times of the world's history and many of the most important remedies to-day are those whose time of introduction is lost in antiquity. In the earliest time, no doubt, our ancestors learnt, as a matter of experience, which plants would serve as food, and which were poisonous. Perchance, it would be learnt, by accident, that the use of a particular plant was beneficial in some disease, or it may be that the medicine-man experimented on his patients with preparations of plants which were not regarded as suitable foods for the healthy. In the course of time the number of plants recorded as having medicinal value has become enormous, but only comparatively few retain a permanent place in medicine.

There are, however, no doubt many valuable natural drugs yet to be discovered, and the work of the investigators of drugs must depend to a large extent on indications given by medical men. I should like, therefore, to impress upon you the importance of gathering information with regard to native remedies whenever possible, and in case you should meet with any that seem worthy of investigation the following four points are worth attention:—Firstly, the complete chemical and physiological examination of a plant requires, as a rule, a considerable amount of material, and even for a preliminary examination a quantity of at least seven pounds is desirable. Secondly, the plant should be accessible in quantity; from the practical point of view, there is little value in finding

out that a plant has useful medicinal qualities, if it cannot be obtained in quantity. Thirdly, it is essential that the plant should be botanically identified, or that a sufficient specimen of its different parts should be collected to permit of botanical identification. Lastly, it is important to record whether the reputed action of the plant in disease is purely of native origin, or whether it has been confirmed by competent observers.

The modern procedure in the case of drugs supposed to have a definite physiological action is as follows:—First, the chemist subjects it to analysis, in the sense of splitting it up into different fractions, and if possible, purifies these by crystallisation or some similar process; then the different fractions are tested in the physiological laboratory to determine to which the characteristic action of the drug is due, and the separated principle finally reaches the clinician.

In conclusion, I should like to express my thanks to Dr. ANDREW BALFOUR, C.M.G., Director-in-Chief of the Wellcome Bureau of Scientific Research, for many interesting suggestions, and to Mr. FRANK TUTIN, of the staff of the Wellcome Chemical Research Laboratories, for his kindly criticism of these notes.

DISCUSSION.

Professor W. J. SIMPSON: I am sure you will all agree with me that we have been particularly fortunate in getting Dr. PYMAN to read a paper such as he has given us to-night. I am afraid it will not bring much discussion, but it is full of valuable information, and its historical interest has been very great indeed.

One was particularly struck with what he said as to the relation between the gum nodules and bacteria, and the spreading of the bacteria by ants and other insects. It has always appeared to me that perhaps we pay too much attention to animals as the source of diseases connected with human beings, and have not paid sufficient attention to the possibilities of the vegetable world being not only the reservoir but the origin of many diseases in the lower animals and man. It has often struck me that when famine or scarcity of food, due to some climatic conditions, occurs, that disease manifests itself in the vegetable world before it begins either in the lower animals or human beings; and I do think, and I have thought so for years but have not had an opportunity

of looking into the matter myself, that there is a possibility, if not more than a possibility, of disease arising in that way in the vegetable world, and being transmitted by insects, or by eating, to the animal world. We know that some of the edible vegetables, such as turnips, cabbages, etc., when affected with rot spreading among them, owe this disease to bacteria, and it is not assuming very much to suppose that such vegetables, when eaten in times of scarcity, may produce disease in the animal world.

I will ask Dr. BALFOUR to open the discussion, as I know that he takes a very great interest in the subject of Dr. PYMAN's paper, and has worked a good deal in this direction.

Dr. ANDREW BALFOUR: On several occasions this Society has "fared foreign" in its efforts to obtain instruction and enlightenment. At such times, I think it is usually the Entomologist who has been asked to provide our mental pabulum. To-night's lecture is, therefore, an innovation, for we have enlisted the services of the Chemist, and, as the PRESIDENT has said, you will agree that we have acted wisely in so doing, for I am sure many of us have heard about things concerning which we were previously ignorant. I am sorry more Fellows are not present to-night to discover their ignorance. Dr. PYMAN has succeeded not only in instructing us but in interesting us. Properly handled, there is no subject more fascinating than that of the origin of drugs, but *materia medica*, as usually taught, is a dismal affair, disliked by the student, and associated in his mind with musty and ill-smelling collections. I have often thought, however, that a book detailing the adventures of drug hunters in, let us say, the great Brazilian forests, would at least be as interesting as a story I once read, called *The Orchid Hunters*, which was full of thrills. After all, drugs unfortunately appeal to a far wider audience than orchids, and it is interesting to think of the travels they undertake and the elaborate processes they often undergo in their conversion from the crude product to the familiar medicine.

Another point on which Dr. PYMAN has touched, is the interesting question as to how the medicinal properties of plants were first recognised. In most cases it was probably by chance, but in others observation and forest-lore must have played a part. I have no doubt

that some of you, in days gone by, used to devour Mayne Reid's wonderful tales. He always managed to present a gilded pill, to combine instruction and amusement. I confess I read him now, upon occasion, and I might do worse. In one of his best South American yarns he describes a battle royal between a snake and a bird, in the virgin forests of Peru. The snake managed to get its fangs home, but the bird at once flew to a vine, from which it plucked the leaves and ate them, recovering its strength, returning to the attack, and eventually coming out the victor. Now, I would be greatly obliged to Dr. PYMAN if he could kindly tell me the name of that plant! It is quite possible that primitive man may also have obtained a knowledge of drugs in some such way, but instinct is a very marvellous thing, and it is certain that wild animals often have recourse to a *materia medica* of their own. You have already heard about the dogs of the forest, whatever they were, and the ipecacuanha. It is possible that they are sometimes wiser than man himself, for one of the strangest of human aberrations was surely the extolling of ipecac.-sine-emetine, which most of us remember very well.

I consider one of the most interesting points brought out by Dr. PYMAN is the partial similarity of configuration of some of the alkaloids of ipecacuanha and opium. I think his suggestion as to the explanation of why opium eaters present a tolerance to emetine is well worthy of consideration. This just shews the value of sometimes calling a Chemist into our counsels.

What Dr. PYMAN told us about chaulmoogra oil is very interesting indeed. It has been used on Providence Island, the Venezuelan Leper Settlement, with excellent results in a few cases, and there is no doubt that chaulmoogra oil, which for a time lay under a cloud, is coming into its own again. I have recently seen a paper by HEISER, in which he employed a mixture of chaulmoogra oil, camphorated oil and resorcin with very considerable benefits in several cases in the Philippines.

The question of gum acacia is specially interesting to me. Gum production is undoubtedly a disease of the tree, and if the tree is in a favourable condition for growth and development, *i.e.*, near a river, it will only produce gum to a small extent. Where you get strong growth you will find little gum. The latter is chiefly produced in desert regions far away from water. You see the native carrying his water

bottle because he has to work far away from any source of water, and the collectors live for days without coming into contact with any water supply.

The point to which Professor SIMPSON alluded is a very important one, and I think it has practically been proved that insects play a considerable part in vegetable pathology.

There are many other questions calling for discussion, but the hour is late, and I see Dr. PAEZ, from Venezuela, is here, and he will no doubt be able to give us some information about the *materia medica* of his country. I should like to thank Dr. PYMAN for his interesting, able, and profitable address.

Dr. FELIX PAEZ: There are in tropical America many popular medicinal plants to which the medical profession until now has paid but little attention. Unfortunately, I have been unexpectedly called upon to speak this evening, and have not had an opportunity of collecting information worthy of your attention; but I should like to say a few words with reference to a plant of which I saw the flower in the Wellcome Bureau of Scientific Research. This plant is known in Venezuela by the name of Rosa de Montana (Mountain Rose). I do not remember now its botanical denomination, but I think it belongs to the Leguminous family. The flowers given in decoction have well-known hæmostatic properties. It is commonly used in all kinds of hæmorrhages, but particularly in hæmoptysis and metrorrhagias and more specially in the metrorrhagia of the menopause, and I think is worthy of study. Physicians in the tropics, except those specially intrusted with official scientific research, have but few favourable conditions for undertaking the study of these plants and their therapeutical applications, though there is a vast field open for useful work.

It is my intention, when I go back to the Orinoco, the flora of which is one of the most interesting in the world, to gather as much knowledge upon these medicinal plants of popular use, so as to be able to afford every information possible to this Society, and I will send, at the same time, specimens of the flowers, seeds, leaves, etc., as suggested by Dr. PYMAN in his important lecture to-night.

Dr. A. T. OZZARD: I have nothing whatever to add in the way of interest to the discussion to-night, but I should like to emphasise the importance of the use of oil of chenopodium in the treatment of ankylostomiasis. It is a drug I have only recently heard about, and towards the end of last year, before leaving Guiana, I started trying it. My numbers of cases were few, but the results were very distinct, and highly in favour of the oil of chenopodium over the results obtained with thymol. Thymol in many ways is disappointing. It certainly improves cases of ankylostomiasis, but takes a long time to cure, and one course is never sufficient; it has to be repeated on several different occasions before you can rid the patient of the parasites. On that account I started trying the oil of chenopodium, and that was certainly the most favourable drug to be found. I would like my colleagues in tropical countries to try this drug, especially now that thymol is practically unobtainable.

Dr. C. F. HARFORD: I think, as a Society, we are very much to be congratulated on the fact that for the first time, so far as I can remember, we have had an expert in chemistry bringing before us the subject of drugs, from the point of view of therapeutics.

This morning I received a Government circular, in common with other practitioners, advising us as to the drugs we should refrain from using, because of their scarcity in this country; owing, I am afraid to a large extent, to the want of enterprise on the part of British chemists in allowing German chemists to monopolise the manufacture of so many of the important chemical products we use in medicine. I hope that the result of the scarcity of these drugs is going to stimulate the activities of our manufacturing chemists. I hope also that it will lead the medical profession to enquire more into chemical products that may be used in therapeutics. This, I think, will be of great benefit to us.

In the absence of the PRESIDENT, I think I must repeat his protest of the last meeting against the statement made concerning ipecacuanha. We all hold in very high honour the first President of this Society, but we must agree with Sir HAVELOCK CHARLES that it is not true that ipecacuanha had been absolutely forsaken by other practitioners, although Sir PATRICK MANSON undoubtedly did much to revive interest in ipecacuanha in certain circles.

I expect we here, in this Society, must have special interest in the preparations of cinchona, but I am afraid that the very familiarity of the subject has perhaps led us to regard it as a subject of which we know everything. This is certainly not the case, and I hope some results may come from the researches recently made with regard to the action of the different alkaloids of cinchona.

I thank Dr. PYMAN for what he said about the collection of new drugs which may have therapeutic value in different tropical countries. I know when I was in West Africa I felt very deeply convinced that the natives of that country did possess a knowledge of many valuable drugs, and I brought home specimens of a good many in order that they might be of benefit to science, but I had no guidance to tell me what I ought to bring. No doubt I erred through only bringing small quantities, but I found great difficulty in getting advice as to how and where they could be tested.

In the department of entomology medical practitioners have received careful guidance as to the specimens to collect, and the manner of collecting, and I think it would be valuable if Dr. PYMAN would give even more-detailed advice to medical men as to what is wanted, and also as to who would deal with these products when obtained. It must also be recognised that to get 7 lbs. of some of the drugs is no easy matter, and if it were known that there were laboratories at home who would be glad to receive specimens of this kind, and that they would be prepared to help in the cost of procuring them, I feel sure a good deal more might be done.

I should like to thank Dr. PYMAN for his valuable and interesting paper.

Dr. F. L. PYMAN: If you will permit me I propose first of all to deal with several points raised by Mr. HOLMES. Mr. HOLMES was not able to be present to-night, but he kindly called upon me this afternoon and gave me one or two notes. In some cases Mr. HOLMES referred to portions of my paper which I have not actually read to-night.

I refer in one place to Borneo camphor. Mr. HOLMES points out that the Chinese prefer Borneo camphor to the ordinary camphor, and as they are a very intelligent people, there is probably some good reason for the preference, which might be worth while looking into.

Then again, on the subject of rhubarb. I say in my paper that the best samples of the drug consist very largely of *Rheum palmatum*. Mr. HOLMES says that the best variety of the drug, known as *Shensi* rhubarb, is characterised by a peculiar rhomboidal network of white lines which is well illustrated in GOEBEL and KUNZE, *Waarenkunde*, Pt. II. taf. 1, fig. 2b, 3b. The only cultivated rhubarb root in which he has found these markings is *Rheum collinianum*, which he has grown in his own garden.

Next, with reference to chaulmoogra oil, I state that Dr. F. PORTER-SMITH mentions that some of the chaulmoogra seeds in Chinese shops appear to be derived from *H. venenata*. Mr. HOLMES very strongly doubts that. He points out that Dr. SMITH confused the seed of *Hydnocarpus anthelmintica*, PIERRE, with the true chaulmoogra seeds, as mentioned in the *Pharm. Journ.*, 19th May, 1900, p. 522.

Then the possible effect of different antiseptics upon gum reminds Mr. HOLMES of a peculiar point. He says formalin might possibly cause a large increase in the amount of gum, because if you take a solution of gum and add formalin to it, it destroys the viscosity, so that formalin might cause the gum to run more freely.

In reply to your kind remarks, Sir, I was very interested to hear of your view that perhaps the vegetable world is first attacked with disease in time of famine.

With regard to Dr. BALFOUR's remarks, I am afraid I do not know the name of the plant which the bird ate of to fortify itself against the attack of the snake. It is a very interesting tale.

With reference to *ipecacuanha-sine-emetina*, as to whether this had any effect in dysentery at all, I think that at the time, when it was so used, it was not known what was amœbic and what bacillary dysentery. It is now known that emetine is specific in amœbic dysentery, but it may be that some other constituent of *ipecacuanha* is of value in bacillary dysentery. Some of the results obtained at that time were due to the fact that the so-called *ipecacuanha-sine-emetina* was by no means always free from emetine.

With reference to Dr. PAEZ's remarks, it is very encouraging to hear of anybody as keen as he is to collect plants.

I was very interested to hear the remarks about oil of chenopodium being actually used by someone present here this evening.

In reply to Dr. HARFORD, it is of course a matter of difficulty for doctors abroad to come into contact with investigators of drugs. No doubt a good many of the Universities and Medical Schools have their chemists and physiologists who work together. There are few other institutions in this country where both are employed and able to give attention to such matters.

TRANSACTIONS
OF THE
SOCIETY OF TROPICAL MEDICINE
AND HYGIENE.

JUNE, 1915.

VOLUME VIII. No. 7.

Proceedings of a Meeting of the Society on Friday, April 16th, 1915,

Dr. F. M. SANDWITH, F.R.C.P., *Vice-President*, in the Chair.

ON AN EPIDEMIC OF AFRICAN TICK FEVER AMONG
THE TROOPS IN BRITISH SOMALILAND.

BY

R. E. DRAKE-BROCKMAN, M.R.C.S., L.R.C.P.

A SHORT ACCOUNT OF THE DISEASE IN BRITISH SOMALILAND.

This disease, from all the information obtainable, only appears to have invaded British Somaliland during the last few years, although the transmitting agent, *Ornithodoros savignyi*, has been known to the Somalis for years. The first occasion on which the disease was recognised was during an epidemic in the coast town of Bulhar during 1912. This epidemic was restricted to a small portion of the community in an outlying part of the town where the indigent section of the townspeople had their huts. The town of Bulhar is the coast town to which in the cold season all the western tribes bring their sheep, skin, etc., for sale, and it appears that the fever spread along this route to the next station, namely, Hargeisa, where there is always a permanent collection of huts belonging to the local mullahs or priests. During the past year,

1914, it was found necessary to send a company of the Somaliland Camel Constabulary to Hargeisa to settle some differences among the local tribes, and it so happened that during their short residences there, a considerable number of the men of this company contracted the disease.

CAUSATION. NOTES ON ORNITHODORUS SAVIGNYI.

On the examination of the peripheral blood of the patients during the pyrexial attacks the spirochæte was found in nearly every case, and all the men practically admitted that they had been freely bitten by the Kudkuda, the local name for *Ornithodorus savignyi*. On examination of the soil among the huts and in the localities where the natives congregated a large collection of these ticks was made.

In British Somaliland, *O. savignyi* is generally found in the soil, in old-standing camps and zarebas, under the shade of trees where human beings and animals are in the habit of resting during the heat of the day, and in the soil around well-frequented wells—in point of fact, every place freely frequented by both men and animals where the soil is light, powdery and dirty. When resting it will lie up in any cranny or crevice in a wall or tree trunk, but seems to prefer burrowing into the soil, as it is a poor climber. When in quest of its victim, it travels rapidly over the surface of the ground and loses little time before it finds a suitable place to drink its fill. It does not seem to have any special predilection for the blood of human beings, but will with equal avidity feed on that of camels, horses, mules, donkeys, sheep and goats.

The mode of progression of *O. savignyi* varies according to the roughness of the surface over which it is travelling. On a smooth surface it usually proceeds propelling itself by its two pairs of hind legs only, with the front pairs folded round on themselves at rest. As soon, however, as obstacles present themselves, or it wants to burrow in the ground, the two front pairs are also brought into action. When turned over on to its back the legs are all folded up at once and it will lie perfectly still until it is satisfied that all danger is passed, and it will then slowly turn over and attempt to make good its escape. It is sometimes said that *Ornithodorus* only feeds at night. This is certainly not the case with *O. savignyi* in British Somaliland.

One has only to stand in any place infested by them to find

within a few minutes that they are swarming over one's boots, while the natives with their naked feet, and the ponies and other animals will become restless owing to their bites, and will be forced to leave the shade of the trees on their account during the hottest hours of the day.

These ticks are more commonly found under trees which provide ample shade both to men and animals during the heat of the day, and it is here that they usually await their victims. They have, however, a better chance of getting their fill of blood from human beings during the night owing to the habit of natives sleeping on the ground in preference to a bed. In native huts where their blood supply is more certain, they probably more often feed at night, as few Somalis occupy their huts during the daytime, whereas under trees and around wells they have a better chance of obtaining a feed during the daytime.

Ornithodoros savignyi always lies dormant just below the surface of the soil, and is probably roused to action by the thud imparted to the ground by the steps of men and animals. Within a few minutes of one's arrival the ground in well-infested areas is found to be alive with them and, whether attracted by sight or sound, they will travel rapidly over the ground in the direction of their blood-supplier. Owing to their dusty, wrinkled appearance they are very difficult to see unless in motion. *O. savignyi* will live for months without a feed, providing it can burrow in the soil. It usually only burrows just below the surface so that it can rapidly emerge as soon as the ground is disturbed by the foot of man or beast. Even in a bottle well corked, so as to shut off all air, these ticks will live for months, and although appearing to be dead on being turned out, they will, within a minute or two on exposure to the air, begin to shew signs of life.

THE SPIROCHÆTE.

During the first two or three days of the initial rise of temperature the spirochætes may be found in the peripheral circulation in numbers proportionate to the severity of the attack. They are invariably seen on the first day in long, thin, regular corkscrews or straight spirals. Very occasionally these straight spirals are to be seen bent on themselves. Two may be seen lying end to end, so as to give the appearance

of one very long spirochæte. Later, on the second or third day, the straight spirals shew a tendency to straighten out and curl into loops.

The spirochætes are seldom difficult to find in the peripheral circulation during the initial rise of temperature or in the first relapse, but in the later relapses they require a good deal of looking for, and are frequently not to be found at all.

CLINICAL COURSE.

Owing to the patients being unattended by a medical man from the date of their arrival on September 25th, in the infected area, until their return to headquarters on October 23rd, it was difficult to arrive at the period of incubation, but the first to report sick with fever did so on the 30th September or 1st October.

The period of pyrexia during the initial attack is usually longer than in the relapses. It may last from 72 to 120 hours, whereas in the relapses it is more commonly from 36 to 72 hours, and in some cases may reach 96 hours.

In this particular epidemic five or six relapses were the rule, but in no case were there more than six relapses.

The apyrexial periods varied from 120 to 384 hours, in other words from 5 to 16 days, but it more commonly extends from 6 to 9 days, and when it extends longer than this there is not infrequently an abortive attempt at a rise for one evening, with a fall to sub-normal on the following morning.

There are a few cases, but these are happily by no means common, in which the temperature seldom rises above normal, and when it does there is a low irregular type of fever which does not often rise above 101°. Except during epidemics, when there are other well marked cases, these are not easy to diagnose. In one case, although a man was suspected of having contracted the disease along with others of his company, it was not until his eyes became affected months after that the diagnosis was fairly certain.

Out of a number of cases which were infected, only ten were badly affected, and these were kept under observation until the relapses ceased. Out of these only three had affections of the eyes, while in only one case were both eyes affected. In these four cases there was iritis, with probably slight opacity of the vitreous, as there

was almost complete loss of sight in the affected eyes for some days.

The liver and spleen were both slightly enlarged and tender in most of the cases. There was a tendency to constipation as a rule, never diarrhoea.

Myalgic pains in the limbs, and particularly severe in the calves of the legs and back, with severe headache, always accompanied the pyrexial attacks and continued more or less severe during the apyrexial periods, when the patients were debilitated and lethargic and had little inclination to work.

Vomiting occurred in most of the cases but not in all, while herpes only occurred in one case, and epistaxis in two.

In no case did jaundice occur, nor were the lungs attacked in a single instance. The heart in all cases was more or less dilated.

PROGNOSIS.

The prognosis, notwithstanding the severity of the epidemic, was very good, no case of death occurring. The disease, however, from a military point of view, is bad, owing to the length of time which usually must elapse before the patient is at all fit to perform even the lightest duties. In most of the cases the patients were unfit to return to their regular duties for three months.

DIAGNOSIS.

In the initial pyrexial attack the diagnosis can only be settled by the finding of the spirochæte in the blood.

In the first and second relapses they are scarce, and usually difficult to find in the peripheral circulation. In only one patient was the spirochæte found as late as in the fifth relapse. In the apyrexial periods the spirochætes are never found in the peripheral circulation. The disease might be taken for subtertian malaria in regions where they coexist, but it can be differentiated by the presence of the spirochæte in the blood and later by the regularity of the relapses.

In those rare cases where there is no rise in temperature, the disease is difficult to diagnose unless there is an epidemic of the disease present, or else after a long period of debility and weakness the patient shews signs of iritis followed by temporary blindness.

PROPHYLAXIS.

Avoid standing about or sitting in the neighbourhood of wells, in bazaars, and tarikas (mullahs' villages), or wherever there is a more or less permanent collection of huts. In places where there are only one or two large spreading trees, under which sheep and goats and human beings rest during the heat of the day, there is always a likelihood of the soil being infested with *O. savignyi*. These ticks don't like being disturbed after feeding, when they burrow into the ground, so they prefer places where filth and rubbish are allowed to accumulate outside towns and villages. In Bulhas, in 1912, I found them in only one quarter of the town, on the outskirts, where the indigent Somalis had erected their huts and shelters.

If a soft tick is touched with a tiny drop of turpentine it will die in thirty seconds or less, so if all the patients suffering from the disease have their legs and feet well rubbed with it they will not be bitten, or rarely so. This is particularly to be recommended when patients suffering from the disease are taken from one locality to another, and so prevent the dissemination of the disease.

METHOD OF DEALING WITH GROUND INFESTED WITH *O. SAVIGNYI*.

When it has been ascertained that any particular area is infested with soft ticks, the best method of dealing with the site is to light a circular fire round the area and then gradually work towards the centre by throwing brushwood into the circle and systematically burning the whole area. This particularly applies to those sites which, for obvious reasons, cannot be abandoned, such as the immediate neighbourhood of wells, which may be few and far between in dry countries. It has been suggested that the ticks will disappear if the ground is sprayed with corrosive sublimate, but this is not the case, owing to the habit of the tick when not feeding, or in search of its victim, of burrowing from half to one inch below the surface of the soil. Experimenting with a 1 in 1,000 solution of corrosive sublimate I found that if the sand containing a number of these ticks of different sizes is thoroughly soaked with the solution and left, the ticks on the following day will be just as lively as before. Furthermore, a young unfed tick can be immersed in the same solution for one minute without its being affected in any way. If

some of the light soil in which these ticks are commonly found is placed in a large glass dish and unfed ticks placed inside and allowed to burrow, the soil can be thoroughly soaked with the solution, and this allowed to dry, when the ticks will be found to be alive and apparently unharmed.

TREATMENT.

Of the various drugs available, the following were tried alone or in combination with no appreciable effect on the course of the disease, namely, quinine, phenacetin, arsenious acid, liq. hydrarg. perchlor., with calomel and magnesium sulphate as purgatives.

DISCUSSION.

Dr. C. J. BAKER : In 1910 some troops went from Uganda to Somaliland and possibly took a spirochæte with them, which may have lain dormant or unrecognised till 1912. The troops were the 4th King's African Rifles, four companies of them. I do not know whether there is any possible connection between the two diseases, therefore, in Uganda and Somaliland.

Dr. C. F. HARFORD : I should like to call attention to one matter of interest arising out of Dr. DRAKE-BROCKMAN's paper on tick fever. When I read a paper before the Society, on the 19th June, 1908, on African Tick Fever, I was able to give results of a series of cases supplied to me by the kindness of Drs. A. R. and J. H. COOK, of Uganda, and one of the points which aroused some interest at the meeting was the reference to iritis as one of the complications of tick fever. In the paper read to the meeting this evening I see that it is mentioned as being a diagnostic point.

Fleet-Surgeon P. W. BASSETT-SMITH : There was one point which I think is rather important, and that was that corrosive sublimate was of no effect for getting rid of the ticks as a prophylactic measure ; one would have expected this would have had far more powerful influence upon them than is apparent here,

The other positive point is the use of turpentine as a prophylactic for people passing from one neighbourhood to another, to prevent an attack being conveyed from an infected to a healthy region.

I would like information on another point. When these ticks get on to a man in East Africa, do they hang on like the ones do in Persia? The common Persian ticks are most difficult to remove. Do these act in the same way? Are they easy to remove or difficult? There is no word about it in the paper. When they are moved, do they leave any local sores?

Dr. G. C. Low: I think I may be able to give Fleet-Surgeon BASSETT-SMITH some of the information he requires. As regards the habits of *O. savignyi* they appear to be different from those of *O. moubata* of Uganda. The latter tick lives in the cracks of the floors and walls of cow-dung houses and huts, and does not occur, at least in any great numbers, in the sandy soil of camping grounds.

O. moubata resembles closely a bug in its habits, coming out and biting at nights, and retiring again at day-light. It does not attach itself and hang on like the ticks mentioned by Fleet-Surgeon BASSETT-SMITH in Persia. The bites are painful, and sometimes give rise to a good deal of local inflammation.

Iritis, though occurring as a complication of tick fever in certain cases, is not a constant feature. When it does occur it is a useful diagnostic point.

Dr. F. M. SANDWITH: I would like to remind Fleet-Surgeon BASSETT-SMITH about corrosive sublimate and plague. When we began to use it in connection with surgery we had great success, and we thought it was the universal destroyer of everything noxious. But when we tried to get rid of plague infection by means of corrosive sublimate in Egypt, it was found that gallons of solution poured on to the floors and walls were of little avail in killing fleas. They minded corrosive sublimate no more than water, it was useless for that, and we had to use other things. Therefore, remembering that experience, it is not astonishing to me to hear that it has no effect on the ticks. The idea was to try and stamp out plague in a village by cleaning all the huts, and the ordinary methods of whitewashing were thought to be insufficient, so that the floors were dug up and a new floor of sand laid

down with a sprinkling of corrosive sublimate, but this did not do away with the infection.

I notice Dr. DRAKE-BROCKMAN talks about various drugs, and I dare say he tried all he had. Of course we know by the experience of others in South Africa that quinine is of no avail. Fellows present will agree that an attack of fever occurring in any man attended by a white doctor would at first certainly be treated in the tropics as malaria, so that probably every case of tick fever that has had a white doctor handy has been thoroughly dosed with quinine.

One drug he does not mention is salvarsan. I should like to ask Dr. BAKER if he has used it? Salvarsan acts as a charm in the relapsing fever of Europe. I am assured that in Petrograd and other parts of Russia they have been able to close certain hospitals which were formerly used for relapsing fever, because one dose of salvarsan will prevent any relapse at all. It is a great advantage if you can prevent the one or two relapses of the European form, or the six, seven, eight, or nine relapses of the East African tick fever.

Then I would like to mention what I believe to be a rare case. A person was sent home to me—a missionary from East Africa—whose blood had been examined by Dr. HOWARD there, and the spirochætes had been found. The attack lasted three or four days. Doubtless the diagnosis was correct. It was her time for leaving for Europe, and she was allowed to leave and told to look out for relapses on her way home. She had no relapse at all, so that was a case with only one attack of fever and no relapse.

We have to remember what Dr. DRAKE-BROCKMAN states, you may have attacks without fever at all. It is quite possible that this woman, who apparently had no rise of temperature, had a relapse. She might have had some slight rise, say 99 or 99½, which she did not discover and would not notice. Still, I think it is rare to have only one attack without any relapse at all.

Another point I would like to ask is, whether in tick fever you may lay it down as an axiom that the spirochæte will occur during the fever and will be absent from the peripheral blood during a pyrexial period. In the relapsing fever of Europe it is found, universally, that the spirochæte disappears from the peripheral blood before the temperature comes down. Supposing for instance the attack lasts seven days, the

spirochæte may not be found on the seventh day. That is important from the diagnostic point of view. Is this true also in tick fever?

Dr. DRAKE-BROCKMAN has been talking about the movement of troops. The cases I have seen from East Africa have generally been white missionaries. I should like to say that the disease there is certainly more heard of in late years than it used to be. I will not say it was not there before, but I think that doctors are more careful. In the old days everything was called malaria. More cases have been reported lately, and the white man and woman are both affected, while the bishop of a diocese and his doctor both got tick fever. They think they got it either from sleeping in rest-houses which are kept for white people, but which are unfortunately occupied in their absence by natives, or from the bed-clothing dealt out from the store by the native storekeeper. It is not enough apparently to keep the rest-houses for white people, but we must see they are not inhabited by ticks as well.

This is a subject about which most of us are ignorant, and if Dr. BAKER will be kind enough to tell us more about the subject, especially about salvarsan, we shall be grateful to him.

Dr. J. M. ATKINSON: If I may be allowed I can confirm your statement with regard to relapsing fever of China being cured by salvarsan. I saw in the Annual Report of Hong Kong that an outbreak which occurred there was stopped quite effectually.

Dr. F. M. SANDWICH: It acts like a charm. It is much more wonderful in regard to relapsing fever than in syphilis.

Dr. C. J. BAKER: I am afraid I cannot tell you much about salvarsan. During the last two years I have been doing sanitary work, not clinical. I do not know of anybody who has tried it except, perhaps, Dr. COOK. It is a very expensive drug and, therefore, I do not think it is practicable to use it indiscriminately. Europeans have usually acquired the infection, when travelling about, at rest-houses in out-lying districts. That may be because the drug has not been tried. Salvarsan is being used out there for syphilis.

As to relapses, I may say there are plenty of cases where there are no relapses. I have had police to look after, and troops. They have

had one attack and often have had no relapse. The last case was that of my own cook, who developed an attack of fever on the road. He had one attack, and we stopped two days for him. He had no further rise of temperature, but had persistent eye trouble for some weeks. The rest houses are the chief places where there is infection, and in the parts where tick fever is prevalent we have burned down camps as much as possible. In camps the native shelters are simply grass huts built for the night; the Europeans have tents for sleeping in. Some shelter is put up for the day, and this with the huts is burned down afterwards. The disease is not so bad as it was. We have labour camps in the stations, which become infested with ticks in time, and they have to be burned frequently. What we want is more permanent buildings for labourers, but we have no money to use for this purpose, so we have to go on with temporary buildings, and burning them down when infested.

As to the disappearance of the spirochætes from the blood, I have found spirochætes in the morning, and in a blood slide from the same patient taken in the afternoon I found none at all, though they were swarming four hours before. The case I am thinking of was that of a native with a high temperature. His temperature was still up in the afternoon, but there were no spirochætes at all although they were swarming in the morning.

FOUR CASES OF BILHARZIASIS UNDER THYMO-BENZOL TREATMENT.

BY

C. M. EKINS, M.R.C.S., L.R.C.P.

(*Director, Alexandria Hospital, Egypt*).

Case I.—Mohamed Ahmed Aly, an Egyptian male, of about 23, a policeman, admitted to hospital on 22nd November, 1914, with symptoms of bilharziasis of the bladder; painful and frequent micturition and hæmaturia. The urine was examined immediately after admission, and living miracidia found.

He was first put on buchu and hyoscyamus, and light diet; subsequently irrigation of the bladder with pot. permang. 1 : 4,000 was started, the bowels being kept all the time freely open.

On 20th December, he was given the thymo-benzol preparation, 0·20 and 15 grains respectively, t.d.s., and this he took for a couple of days, during which period he was more or less intoxicated.

The dose was reduced for this reason from 15 grains to 4 grains, and the patient continued to take 4-grain doses t.d.s. for six days, and three more searches in the urine on different days proved the persistence of active miracidia. Bowels regular, no alteration of pulse.

Patient discharged on 31st December, unimproved.

Case II.—Ahmed Mansoor Admed, an Egyptian male of about 35, labourer, was admitted on 16th December, 1914, with straining at stool with blood and mucus. Stools examined and bilharzia ova found, urine searched and living miracidia also found.

The patient's bowels were first opened by a dose of sod. sulph.; felix mas was then administered internally, and tannin enemata for two days.

On 19th December, he was given the thymo-benzol treatment, 0·20 of the former and 15·00 of the latter, four times daily, but symptoms of intoxication supervened. (The patient kept laughing and was full of hallucinations). This big dose had to be reduced next day to 4 grams only t.d.s.

Meantime, repeated examinations of the stools and urine proved positive, active miracidia present. The treatment was continued until 26th December, and, one more examination of the fæces and urine proving positive, this case was sent out on 3rd January, 1915, no better.

Case III.—Mohamed Aly, a boy of 12, Egyptian, admitted on 19th December, 1914, with symptoms of dysentery, the nature of which was revealed by a microscopical examination of the stools which proved the presence of ova and miracidia.

On the 21st and 22nd, patient was given small doses of calomel, which acted well, producing four or five lax motions in the 24 hours.

On the 23rd, he was given the thymo-benzol, 0·20 of the former and 3·00 of the latter, t.d.s., which treatment he kept taking for six days, the bowels open all the time. Except that the boy was slightly drowsy, there has been no change worth mentioning.

Result.—Miracidia which were alive on the first examination, were not found on a second examination made on the 24th, and another on the 26th, but in repeating the search on the 28th, a few living miracidia were found. The boy was discharged on the 31st, unimproved as far as the bilharzia is concerned.

Case IV.—Aly Soliman, a policeman of about 22, admitted on the 18th December, with a complaint of passing blood and mucus in his stools. For two days his bowels were opened by 10-grain doses of sod. sulph. in the morning at the time that his stools were sent to the bacteriologist, who reported absence of bilharzia and presence of ankylostoma ova. The patient was put on the thymol treatment for ankylostomiasis, while tannin enemata were also administered. Bilharzia ova were looked for again next day, but neither they nor amœbæ were found.

Three days later, a further search in the stools still proved absence of bilharzia ova and amœbæ, but revealed existence of trichomonas. Next morning, *i.e.*, on the 24th, bilharzia ova were found, though not one miracidium out of the shell. On the 26th, another examination proved negative to both bilharzia and trichomonas.

Before starting any thymo-benzol treatment the stools were examined once more, on the 28th, this time living miracidia being found; the patient was given six doses of the preparation in two days, 0·30 of the thymol and 3·00 of the benzol. The amount of blood passed per rectum next day was even worse than before, and on further examination living miracidia were again found.

The patient, a policeman, was eventually discharged from the service.

Dr. F. M. SANDWITH: As this paper was sent to me I would like to tell you its previous history. About a year ago Dr. WILLIAM ROBERTSON, of Natal, whom I have not the pleasure of knowing, wrote to me and told me he had discovered a cure for bilharziasis. As you know, there is no known cure for that disease, and I was very pleased to hear of a cure for it. Shortly afterwards he sent an extract from a lay paper, published in Natal, to one of the Secretaries of this Society, and it was published in our TRANSACTIONS in Nov., 1914. It was stated that it invariably cured the patient, and, curiously enough, he said in the paper that the patients never suffered from intoxication. I am always pleased to hear of any cure, but I like to have it confirmed, and therefore I wrote to Egypt and asked whether they would mind trying this treatment and letting me know the result. Then the war came and I did not hear anything; so I wrote again, and had a reply that they had not tried it in Cairo, but that Dr. EKINS had tried it in Alexandria and found it of no use. They said they would send me his paper, and they sent this paper you have just heard, which is now open for discussion. Dr. EKINS found these four cases were not benefited by the drug, and he wrote to say that the intoxicating effect was a great nuisance, because you always had to be holding the patients down in their beds. Now it rests for you to decide between the two experiences of Dr. ROBERTSON and of Dr. EKINS who found no advantage in using the drug.

Fleet-Surgeon P. W. BASSETT-SMITH: There was a paper by Dr. ROBERTSON, a short time ago, in the *British Medical Journal*, which no doubt a good many read, and it is an extreme disappointment to find that what appeared to be very important statements are of doubtful value. It certainly seems that not only is the drug unlikely to do good but it may possibly be harmful, and anyone reading the article in the *British Medical Journal* would be led into error.

Dr. FELIX PAEZ: Thymo-benzol has been used in Caracas with very good results by Dr. GONZALEZ RINCONES in the treatment of bilharziasis, according to the formula of Dr. ROBERTSON, from Natal. This consists in a mixture of one gram and eight centigrams (1·80) of benzol and of fifteen centigrams (0·15) of thymol. Some cases have yielded to this treatment.

Dr. F. M. SANDWITH: I do not know whether the meeting would be interested in hearing that many years ago, when I first learnt that thymol was useful for ankylostomiasis, I hoped it would be of some use for bilharziasis; and I gave it in all the doses I knew how. I often gave small doses of three grains three or four times a day. I did not give the benzol with it. Dr. ROBERTSON in his original paper wrote that he first of all tried thymol and found it of value, then he added benzol with very great success.

Fleet-Surgeon P. W. BASSETT-SMITH: I was in hopes that this treatment might have been of use for schistomiasis in China, which is due to the *S. japonicum* parasite and which disease is still more unfavourable to health than the bilharziasis in Egypt. One hoped the drug could have been used in China for this disease, especially as there is no known cure for it at present.

THE TREATMENT OF ANKYLOSTOMIASIS IN VENEZUELA.

BY

C. E. F. MOUAT-BIGGS, D.T.M. & H., CAPT. R.A.M.C.

Popular treatment of Tricocefalosis and Aquilostomosis, Suionimea, Hipatera, Chimbombera, Jipatera, Tuibombera, Tun Tun, Tungila, Tropical Anæmia, Uncinariosis—a great variety of synonyms.

This treatment, used in many countries of Tropical America (Costa Rica, Colombia, Venezuela, etc.), is very simple, practical, harmless, and truly astonishing in its results. In Costa Rica, it is believed that it will put an end to that terrible disease, if people continue to use it in cities, villages and farms. The treatment consists simply in taking for three consecutive days a spoonful of milk of the higueron (*Ficus laurifolia* family *Moreas*), in the morning, mid-day and night, mixed with water, plain or sugared, or with cow's milk. On the morning of the fourth day the patient must take 30 grammes (practically one oz.) of Glauber's salt (sulphate of soda), but if this is not handy, Epsom salts will do instead. When there is no one who can examine the faeces to ascertain if ankylostome parasites or eggs are still present, the treatment is repeated two or three times with intervals of one month, till the patient is quite cured. The dose for an adult is as follows:—

Milk of higueron, 30 grams.

Aqua pura or cow's milk, plain or sugared, q.s.
to be repeated t.d.s., at morning, mid-day and night.

For children, the dose of the purgative must be less according to age, in the following proportions:—

For children of 15 years	...	15 grams.
„ „ 10 „	...	10 „
„ „ 5 „	...	5 „

The dose of the milk of higueron for children must be half a spoonful each time.

This is the treatment now adopted entirely by the National Board of Health for the entire suppression of ankylostomiasis in Venezuela.

Dr. F. M. SANDWICH: I should like to ask whether higueron is a word used for any kind of fig, or whether it is a special kind of fig?

Dr. FELIX PAEZ: The latex of higueron is really useful against ankylostomiasis, but its action is more powerful against tricocephalosis. The tricocephalus is not so harmless, and it is believed that it can give rise to diarrhœa, a dysenteric condition, and general anæmia. The value of higueron will be appreciated when one considers that up till the present day we have not had any drug which will cause the expulsion of the whip worm from the intestine.

The higueron is a very handsome tree, which sometimes attains to a height of eight to ten metres. Botanically it is known as *Ficus glabrata*, and belongs to the family of the *Moraceæ*, order *Urticales*. Its fruit is much like the European fig (*Ficus carica*).

Other trees of the same genus have the same properties, particularly *Ficus doliaria*, which is generally used by Brazilian physicians.

The latex is collected by making incisions in the bark. It has a syrupy consistence, a milky aspect, a styptic taste, and mixes easily with glycerine and water.

The latex has a mild aperient action. It is not dangerous, nor does it cause unpleasant symptoms. It is given in doses from ten to forty grammes, according to the age of the patient, mixed with milk or sweetened water.

The best plan is to give on the evening before a saline purge, then early the next morning the latex, which is then followed two or three hours afterwards by another purgative.

This cure may be repeated every week till the complete expulsion of the parasites. Three to four courses are generally sufficient.

How the latex acts has not yet been ascertained.

Dr. F. M. SANDWICH: Of course we are very ignorant about the value of these various figs. Figs were used ever since days immemorial to soothe the outside of the body. We don't know much about their use internally—*Ficus doliaria*, MART, juice has been used in Brazil for dozens of years against this very disease we are talking about. The suggestion now is that this new fig is probably as good or better than the

old fig. *Ficus anthelmintica*, MART, gained its name on account of its being prescribed successfully against tapeworm. It is obvious that if there are two or three kinds of vermifuge figs they should not be neglected, as any of us would be glad to be supplied with a better drug than thymol if we can get it, especially just now, when thymol can hardly be procured.

BUBA, OR *LEISHMANIASIS AMERICANA*, IN PARAGUAY.

BY

* DR. L. E. MIGONE, ASUNCIÓN, PARAGUAY.

During recent years a disease called buba has appeared in the north of Paraguay, among the native workmen in the large industrial establishments of these regions, in the Yerba Maté plantations, and in the lumber forests. The condition is an ulcerating affection, of a chronic nature and slow development, which attacks the uncovered parts of the body—the feet, the legs, the arms, neck, and face—and later invades the mucous membranes of the nose, pharynx, larynx, palate, and lips. This disease has very likely spread to this country from the neighbouring state of Brazil, where it has long been known to exist. At the present time, owing to a lamentable negligence on our part, these ulcers are appearing in our territory to such an extent that, according to the evidence of patients coming from these districts, hardly a house can be found in which one or several cases of the disease do not exist.

The disease has been observed in natives of the country, and in foreign residents; in men and in women, in the old, and in infants at the breast. There have been years and districts in which it has caused terrible havoc. Of one hundred workmen who entered the woods to work, seventy to eighty of them had to leave within two months owing to the development of ulcers, in many instances in large numbers spread all over the body.

In Paraguay, as in all other countries where buba exists, the malady has been considered to be identical with syphilis, but of a kind not at all amenable to ordinary specific treatment. From this mistake in diagnosis, of course, the etiological study of the disease was neglected, and its treatment for the same reason was fruitless; and so it has continued spreading.

Medical men, seeing these cases for the first time and not considering the pathology of diseases peculiar to these countries, may often confound

* "*Revista Médica*," Asunción, Paraguay, January, 1914.

it with syphilis, leprosy, sporotrichosis, cancer, etc., and this more especially when it is seen in the later stages, when the nasal and pharyngeal mucosa have been attacked.

In recent years much has been published regarding the disease, both in Brazil and in Paraguay, especially with the object of its differential diagnosis from syphilis. Nevertheless, in all the classical works on tropical diseases and dermatology, buba is confused with "pian," frambæsia or yaws, or other such tropical ulcers. Now, however, thanks to modern methods of research, it is possible to differentiate diseases formerly confounded, and also to unify the different names given to one and the same disease in different countries. In Paraguay the name given is "Buba"; in Brazil, "Bouba"; in Bolivia and Peru, "Espundia"; in Colombia, "Úlcera Torrealba"; and I believe that the "Úlcera de Baurú," of PARENHOS, the Leishmaniasis rhino, bucco-pharyngeal, of SPLENDORE and CARINI, etc., etc., are all the same disease with the ulcerations of the skin and nasal, buccal, and pharyngeal mucosa. They are one single disease produced by one specific kind of leishmania.

ESCONEL, of Arequipa, has given a good description of the clinical manifestations of espundia of Peru, and LAVERAN and NATAN-LARRIER have described the specific leishmanial agent of the infection under the name of *Leishmania tropica* var. *americana*, and LAVERAN has proposed the name of *Leishmania americana*.

In Paraguay, we have had the opportunity of studying the disease in all stages of its development. We have seen it in its first or cutaneous stage, when the ulcers are found on the cutaneous surface of the extremities, the neck or face, and when they may easily be confused with the ulcers of biskra or aleppo, or even with syphilis. Generally the disease begins with one or more erythematous papules, which are very itchy, as if they had been caused by bites of insects. Two or three days later, one or more of these papules becomes purulent, the pustule being about the size of the head of a pin. When the pustule bursts, as it does very soon, it leaves a small hole from which there exudes a sticky, serous fluid, which, on coagulating, forms a dark greyish scab.

In the districts where these ulcers occur there is a general belief that they are caused by the bites of ticks, and, indeed, nearly all the patients we have examined blame the ticks as being the originators of their sickness. I have, however, seen patients whose initial sores have

appeared on the face and the ears, as results of the bites of mosquitoes and horseflies, or other insects. I have seen others in whom the sores have developed from scratches of thorns on the sole of the foot. I have never seen them develop on the hairy scalp, and it appears as if there must always be some solution of the continuity of the skin for the virus to penetrate and originate the disease. The ulcer, once started, rapidly extends, covered by a dark, thick, hard crust, while the surrounding skin becomes congested and slightly œdematous. The initial itching soon passes, and the ulcerated part remains more or less painless. When the scab is pressed there exudes from the sides a foetid, purulent serum. From the ulcers there originates a lymphangitis, the affected lymphatics forming hard, reddish cords, and if these are pressed in the direction of the ulcer, the sero-purulent discharge comes bubbling out. Here and there on the affected lymphatics are found thick, hard nodules, which later burst and form new ulcers. When the crust or scab is removed there is seen a red, fleshy, papillomatous base, which readily bleeds. The margins are clean cut with no undermining, livid in colour, thickened and slightly elevated above the surrounding skin.

These ulcers often cure spontaneously within seven or eight months, leaving a cicatrix of irregular form, parchment-like in the middle, and translucent, so that the little vessels shine through. This scar is very characteristic. The lymphatic glands are painful at the beginning, but later the pain disappears. The glands never recover their normal size. Of general symptoms there is nothing very special—slight evening temperature, joint pains, headache, and these only during the period of cutaneous infection. Such ulcers as do not heal spread slowly, sometimes rising above the level of the skin, forming fleshy, fungating masses, from which there is a continuous serous discharge, and over which no scab forms. These are the “moist lardaceous bubas”; others remain dry and covered by a scab, these are called “dry bubas.” The ulcers vary in size from the size of a shilling to that of a five shilling piece, although sometimes the whole of the dorsum of the foot may be involved, or the whole of one side of the leg or arm.

At the end of two or three months later, that is, in five or six months from the original inoculation of the disease and the appearance of the primary papule, there begin to appear the lesions of the nasal and pharyngeal mucosa. This is the second or mucous stage.

When the initial sore is on the face, then the nasal mucous membrane gets affected very soon. Cases are sometimes seen of unfortunate people, who, within two or three months after the cure, and more or less complete cicatrization of some quite insignificant sores, begin to develop ulcers on the nasal mucous membrane. There is first noted a slight difficulty in the nasal respiration, the pronunciation becomes nasal, and soon there appears a sero-purulent discharge with an occasional tinge of blood. On examining the nasal mucosa it is seen to be infiltrated and reddish, covered with a yellowish crust, especially on the nasal septum. The ulceration continues and frequently there results perforation of the septum. The infiltration spreads, and soon the patient feels a roughness and dryness of the throat and soft palate. The mucous membranes slowly hypertrophy in thick, granulating masses—the pillars of the fauces, the tonsils and the uvula. The patient has difficulty in swallowing solids. Later there come cough and hoarseness as the larynx becomes infiltrated and the vocal cords covered with granulations. Thus, when one examines an advanced case of the disease, there is found this general infiltration of the mucosa of the throat with characteristic granulomatous growths.

After the destruction of the nasal septum the outer nose itself is affected, becomes reddened and thickened, hypertrophied and oedematous. The upper lip is likewise invaded by the same infiltration, and the hairs fall out, and the skin of the cheek-bones also becomes infiltrated and congested. When the nasal mucous membrane has become ulcerated, and the skin at the margins of the nostrils and the skin of the cheek-bones and lips, the affected tissues are replaced by granulating masses, sometimes dry, sometimes moist, just like a true ulcerating lupus, with which indeed it is often confounded.

In proportion as the ulceration proceeds externally, so also internally the mucosa go on thickening with granulations, to such an extent that the soft palate, the uvula, the fauces, and the tonsils form one common mass of red, fungating tissue, that bleeds with the greatest readiness. The isthmus of the fauces gets blocked up, and the pharynx and the larynx become occluded, and speech and nutrition become impossible. The teeth become attacked with a periostitic infiltration and a secondary alveolitis. Even in the most advanced cases lesions of the tongue, or the digestive organs, or true osseous lesions from extension of the disease are never seen.

The patient may live ten, fifteen or twenty years, the infiltration gradually extending to the bronchi until septic fever, malnutrition and exhaustion end in death. This is the end of practically all the cases of buba that have not taken the precaution, or had the opportunity, of being cured of the initial ulcer. All the advanced cases with the naso-pharyngeal lesions will, without exception, shew the cicatrix of an initial ulcer, dating some two or three years previously.

ETIOLOGY.

We have already mentioned, as stated by the patients themselves, that it is a tick of some kind that inoculates the virus. We have, however, attended patients with ulcers that have not been due to the bites of insects, but have developed after some slight excoriation of the skin, caused by the nail of the hand, or from thorns, as if it were the case that the virus awaited some solution of the continuity of the skin in order to penetrate and develop the disease.

When we examine the pus which exudes from the sides of the scabs in recent cases, it is very easy with appropriate stains to determine the presence of numerous leishmania bodies, the big epithelial cells chiefly containing them. This parasite is very similar to the bodies found in the biskra and aleppo sores, and, indeed, the biskra sore has been shewn by ULYSSES PARANHOS to be identical with the baurú ulcer investigated by him, and which was probably a case of buba in the first stage.

In the advanced cases it is difficult to detect the presence of leishmania, but they can always be found. In one case a little lymph was drawn by a syringe from the granulating tissue, and the leishmania easily detected. I have in this way been able to find the same bodies as those found by PARANHOS, CARINI, SPLENDORÉ, etc., in cases similar to my own.

I have not been able to inoculate the disease in animals. I have experimented on the dog, cat, and monkey, without obtaining any definite results. I have examined cutaneous lesions in dogs in the houses of labourers who work in the infected regions, but have been unable to find leishmania; nor have I been able to find them in their blood.

It is also worth mentioning that leishmania are not to be found

in the blood of the buba patient. I have tried cultures in appropriate media but without result, probably owing to faulty technique.

PATHOLOGICAL HISTOLOGY.

The examination of some of the growths in their first stage, and of others after complete development, demonstrates the character of the changes in the subcutaneous tissues and in the skin proper. The dermis is œdematous, the malpighian papillæ are flattened out or lengthened and separated from each other by the œdema. The papillæ nearer the infiltrated dermis are seen extending deeper, until in the infiltrated area they have completely disappeared. The inflammatory exudation is characterised by an accumulation of small cells, lymphocytes and polymorpho-nuclear cells towards the extremities of the malpighian papillæ, as if it was there that the virus settled. Gradually the cellular infiltration becomes denser until it forms quite an inflammatory nodule, the papillæ disappear, and only the remains of epithelial structures are to be found among the invading cells. The same happens with the cells of the sweat and sebaceous glands. Once the basal layer of the epidermis is destroyed, the process proceeds rapidly and an ulcer forms. The capillaries and lymphatics dilate; the endothelial cells are easily distinguished, and the parasites seen in them.

We have not been able to detect the formation of giant cells even in the most advanced cases. FRANCHINI, of the Pasteur Institute, found giant cells in a case of "Ulcers Buba del Brasil," but these may have been the result of some bacillary infection. For colouring and fixing I have used the GIEMSA and SCHAUDINN solutions, and xylol acetone for decoloration.

For the diagnosis of the leishmania it is necessary to take a scraping of the granulating tissue, or to examine the discharges that come from the margins of the scabs or aspirate with a syringe.

TREATMENT.

In the initial stages the treatment is very easy—caustics, thermocautery, and potassium iodide and arsenic by the mouth.

In advanced cases the treatment is very difficult. Extensive cauterisations with the actual cautery, and "606" have given good results, but the treatment must be repeated on three or four consecutive occasions.

When the disease has invaded the mouth and nose it is very intractable. Considerable improvement results from the use of hec tin, "606," orsudan, soamin, etc., but the resulting cure is slow, and has to be supplemented by local caustics. The granulations of the mucous membranes offer little resistance to the thermocautery, melting away like butter.

It ought to be mentioned that even after three or four injections of "606," the parasites are still to be found, and even after three months of treatment with soamin, indicating that in all probability these arsenical products have no specific action upon these protozoa

FURTHER INVESTIGATIONS ON THE ETIOLOGY OF *LEISHMANIASIS AMERICANA.*

BY

* DR. L. E. MIGONE, ASUNCIÓN, PARAGUAY.

We have already, under a similar heading, published in the first number of the *Revista Médica* an article on "Bouba," a chronic ulcerating disease prevalent in the northern forests.

In Brazil, where the disease has been known for many years, it has excited the interest both of the Brazilian medical men and of the foreign hygienists who have visited that country.

In the December number (No. 10, 1913) of the *Bulletin de la Société de Pathologie Exotique de Paris*, there appears a long article on the Etiology of Buba, by Drs. E. BRUMPT and A. PEDROSO, Professors of Parasitology of the Faculty of Medicine and Surgery of São Paulo, Brazil.

In the first place, they, like ourselves, accept as synonymous the different names "Pian Bois," "Forest Yaws," "Bosch Yaws," "Bouton de Bahia," "Ferida Brava," "Ulcère d'Avan Landava," "Bouba Brasileira," "Ulcère de Baurú," "Ulcère de Nordeste," "Espundia," "Ulcera de Torrealba," etc., names given by different authorities in the different countries of America to one single disease produced by a leishmania, the *Leishmania americana*.

In the second place, basing their theory on three well-authenticated characteristics of the disease, they attempt to solve the problem of its etiology, which has until now been very little studied.

These three points are (1) That the disease is common in the virgin forests; (2) That it attacks the uncovered parts of the body only; (3) That it is most frequent in certain seasons of the year. (According to FLU, of Surinam, the disease is contracted from November until April, which may indicate something regarding its entomology.)

The writers offer numerous hypotheses to explain the inoculation of the virus, but can record very few experiments made with a view to explain its natural transmission, or its etiology.

* "*Revista Médica*," Asunción, Paraguay, March, 1914.

In Panama, DARLING studied a case in which the patient blamed the bite of a tabanid. DARLING believes in the possibility also of its inoculation by mosquitoes, fleas, ticks, bugs, flies, etc.

In Manáos, A. MATLA blames an ixode, *Dermacentor variabilis*. In Paraguay it has been attributed to the *Amblyoma striatum*, *Amblyoma fossum* and the *Amblyoma cajennense*. FLU, of Surinam, also holds that the ticks are the carriers, while FRANCHINI says that it is a Brazilian fly, commonly called *Cotunga*.

With the object of determining which of the above-mentioned families are the true inoculators of the disease, BRUMPT and PEDROSO made an excursion into the woods where these cases of leishmaniasis abound. This was in the month of September, 1913.

Starting from the facts already enumerated, viz., that the affection is contracted in the virgin forests, and that it is the uncovered parts of the body that are attacked, it is logical, they say, to think that the disease exists in an endemic state in the bodies of some wild mammals, or in the bodies of some insects, that in certain seasons of the year accidentally inoculate man or animals. Considering the distribution of the ulcers in the body, it is not possible to think that they can be produced by insects that adhere to those parts, but rather by such as bite momentarily. Is this insect, then, one of the Hæmatophaga, or is it any kind of fly whatever that may mechanically convey the virus? The writers have collected specimens of leeches—that of the genus *Hæmadipsa*—which attack men in tropical regions and in the woods, but these leeches are not even known to the patients examined, and, moreover, they are very rare in Brazil. Their rôle as transmitters of the disease in Paraguay is very doubtful, and is not recognised.

Of the common Acarina, the family of the Argantinæ, which rarely bite man, the Ixodinæ, which very commonly bite him, whether in their larval or adult state, are both eliminated by the authors because, they say, dogs which are very liable to the natural infection, and are frequently attacked by ticks, present the ulcers on the nose, a place where the ticks never adhere. The ulcers scattered about on the upper and lower extremities are much more likely to be produced by inoculations of insects that bite several times in succession, such as the hemiptera or the diptera, and not by ticks which always remain adherent to the skin.

Which of the Hemiptera can it be? The pediculi of the head or body are excluded. Bed bugs (*Cimex lectularius* and *Cimex rotundatus*) cannot be the inoculators, as they are very rare in the woods. It cannot be the *Conorrhinus Triatoma*, Barbeiro or Vinchuca, which in Minas Geraes transmits the disease of Chagas, as these insects prefer inhabited places, and not the heart of the woods where the leishmanias abound.

Of the Diptera, the authors studied (1) one of the pupipara which lives on deer, but which rarely bites man, (2) fleas which are very common on forest animals, and (3) chiggers, all of which produce lesions, which do not, however, correspond to the distribution of the ulcers of buba.

The authors themselves consider that the Tabanidæ are the most probable hosts and inoculators of the virus; but they are unable as yet to give adequate proof. The Simulidæ and the Phlebotominæ are likewise blamed, but without reason. So also the Culicinæ and the Anophelinæ. The work of these authors has not been of the nature of laboratory research or biological experiment such as might prove the existence of a larval or latent leishmaniasis in the carnivora, ungulata, rodentia, or edentata which abound in the virgin forests, or the permanent or temporary existence of leishmania in the insects that most commonly surround the men during their work. It would be necessary also to make a study of the cutaneous surface of the woodman after several days' residence in the woods where the infection is endemic.

In our own article on buba we have already pointed out that we have seen the initial lesions develop on the ears and on the cheek bones after bites by mosquitoes, horse flies, and other insects. At other times we have seen them develop in insignificant cutaneous abrasions, or from the pricks of thorns on the sole of the foot, as if all that were necessary for the penetration of the deadly virus were some simple solution of the continuity of the skin.

To sum up: We know nothing categorically so far of the etiological phenomena of buba except by assumption from the facts already given. It is necessary, therefore, still to continue our search for the origin of the leishmania, the pathogenic agent of buba, and this can only be arrived at by prolonged expert entomological and laboratory investigation on the spot.

Dr. G. C. Low: I should like, in opening the discussion on Dr. MIGONE's two very interesting papers, to make one or two remarks in regard to treatment. I see, for example, that no mention of intravenous injections of antimony is made in this respect. The late Dr. GASPAR VIANNA has lately shewn that such injections are very beneficial in the treatment of ulcerating granuloma of the pudenda, and if the results which he claims to have obtained are eventually confirmed, one of the most wonderful advances in therapeutics in recent years will have been made, as up to the present time no drugs or local treatment have been found to be of any value in this terrible disease.

I mention the treatment of ulcerating granuloma with intravenous injections of antimony especially, because similar treatment has recently been tried in South America for local and general forms of leishmaniasis.

I was speaking to Dr. WENYON, lately, on this subject, and he told me that such injections were said to have a very beneficial effect upon local lesions, but did not cure the ulcerating lesions of the pharynx and the nose. Still, as Dr. MIGONE has pointed out, if the local lesions are quickly treated and removed, general lesions may not necessarily follow.

A recent French paper in the *Bulletin de la Société de Pathologie Exotique* gives the results of a similar line of treatment in infantile kala-azar. Cases are there reported with apparently beneficial results from such injections. This is very interesting, because you all know that the treatment of trypanosomiasis with antimony has often been successful, and probably forms the most beneficial treatment for that disease we at present know of.

I remember seeing forest yaws in British Guiana. In those days wood cutters who went into the primeval forests used to get such ulcers on their hands and arms. Some of these resembled a tumour sort of growth, and did not necessarily ulcerate. In some of the cases when the growths were small and not numerous one excised them surgically. It is now, of course, known that forest yaws is but a variety of American leishmaniasis, as MIGONE and others have pointed out.

Fleet-Surgeon P. W. BASSETT-SMITH: I have no experience of the actual disease. With regard to the leishmaniasis itself, it seems that this is due apparently to a leishman body of a closely allied species. The Eastern variety has to go through a flagella form, and it seems almost a

DISCUSSION.

certainty that the species in South America has probably the same life history; and it is almost certain that at some time it has to go through a secondary host, and that host, whatever it is, is a biting one which probably bites exposed parts and does not rest long. It is unlikely that man is infected by injuries to the skin. It must be through some secondary host.

Dr. Low mentioned about the antimony treatment in the case of Mediterranean kala-azar; this and arsenical drugs are, I believe, very important. A case of my own, continuously under treatment, received over 500 grams of arsenic spread over two years. The case has gone out well. The patient was told to report if he had a relapse, and as I have not heard from him I presume he is still doing well. When he left the hospital his blood had become normal in appearance. He gained in weight. He had continuously, twice a week, the treatment as Sir PATRICK MANSON advised. We saturated his system with small doses. It cured the leishmania in this man, and so it is one of those treatments that might be useful in the American form if continuously applied.

The man had albuminuria for a short period, which cleared up when the drug was omitted, after which he again resumed the treatment without further trouble.

Obituary.

PROFESSOR ANGELO CELLI.

ANGELO CELLI was born at Cagli (Pesaro, Italy), in 1857. He studied medicine at the University of Rome, and after taking his M.D. degree remained there as Assistant to TOMASI CRUDELI. In 1886 he was appointed Professor of Hygiene at the University of Palermo, and in the following year founded a Pasteur Institute there—one of the first in Italy.

In 1888 he returned once more to the University at Rome, and for twenty-six years—up to the moment of his death—he continued to work there, honoured by his colleagues and venerated by generation after generation of students. The subject with which his name is chiefly connected is malaria, his valuable work and researches on this subject being so well known as scarcely to need comment. In addition to this he studied jointly with MARCHIAFAVA the etiology of cerebro-spinal meningitis, isolating a coccus, which was later on more completely described by WEICHELBAUM. His work on dysentery, cholera, diseases due to ultra microscopic viruses, and many other infectious diseases is well known. He devoted a great deal of time and work to practical hygiene, examining the water in various districts, including that of the subsoil of Rome, etc., and made important physiological studies of the food used by the peasants in various parts of Italy. He also compiled a most important experimental study on the hygienic conditions of the workers in tobacco manufactories, and caused an enquiry to be made into the subject. It may be also remembered that CELLI was among the very first to call attention to the importance of flies and other insects in the dissemination of disease.

Known amongst his colleagues throughout the world as a great scientist, it is as a philanthropist that CELLI will be best remembered and loved in the agricultural districts of Italy. In conjunction with his wife he founded several schools for the Contadini of the Campagna, and also out-patient dispensaries in Rome. In 1892 he became a Member of Parliament, and in this capacity he contributed greatly to the betterment of the agricultural population. In addition to causing

a law to be passed for the free distribution of quinine to the poor, he was instrumental in passing other bills for the improvement of sanitation in the Campagna and other agricultural districts. His memory will always be revered by his colleagues, his disciples and all those acquainted with his work.

Professor CELLI was appointed an Honorary Fellow of the Society in January, 1910.

WILLIAM SANDILANDS HARRISON, M.B., C.M. (GLAS.),

LIEUTENANT-COLONEL R.A.M.C.

Lieutenant-Colonel WILLIAM SANDILANDS HARRISON, R.A.M.C., died at Haslingden, Lancashire, on April 12th, 1915. Born on March 15th, 1872, he was educated at Glasgow, where he took his M.B. and C.M. degrees in 1893. He entered the R.A.M.C. as surgeon-lieutenant on January 29th, 1895: became surgeon-captain on January 29th, 1898, major on July 29th, 1906, brevet lieutenant-colonel on July 4th, 1914, and lieutenant-colonel on March 1st, 1915. He served in the 'Tirah campaign, on the North-West Frontier of India, in 1897-98, receiving the medal with two clasps. He had recently held the post of assistant professor of pathology at the R.A.M. College, Millbank, and lately had been serving in Jamaica.

Sir WILLIAM LEISHMAN, writing of his old friend (*B.M.J.*, April 24th, 1915), rightly states that "the Royal Army Medical Corps has lost an officer whom it could ill spare, and for whom, had he lived, high honours and distinctions would most certainly have been in store. There can have been no officer in the corps of his standing who was more universally respected and liked, both for his exceptional professional qualifications and his sterling character. A sense of personal bereavement must be strong in all who knew him and read of his death. Sir WILLIAM LEISHMAN had the privilege of the closest association with him as a fellow worker in the Royal Army Medical College for many years, and was under a heavy obligation to him for loyal and untiring co-operation, both in research and in teaching; the passing years served but to strengthen a feeling of admiration and respect for a character and

intellect of exceptional strength. The research work accomplished by Lieutenant-Colonel HARRISON in many lines is of great and permanent value, notably his important share in establishing typhoid inoculation upon a firm and scientific basis. His appointment to the Chair of Tropical Medicine at the Royal Army Medical College proved an immense success, and furnished an instance of that rare but admirable combination—a clinical observer of exceptional experience and insight armed with a full practical knowledge of modern laboratory methods. It was a hard stroke of fate which denied to him the chance of serving his country at this time, and one which he felt bitterly, but the fortitude and calm courage with which he endured his painful illness and faced the inevitable will not readily be forgotten by those whom he honoured with his friendship.”

Lieutenant-Colonel HARRISON took a great interest in tropical medicine, and was a very constant attendant at meetings of the Society. In June, 1913, he was elected a member of the Council, and while serving in this capacity he took an active part in the interests of the Society, interrupted only by the fact of his having to go to Jamaica. The Society has lost a Fellow for whom, as Sir WILLIAM LEISHMAN says, high honours and distinctions would most certainly have been in store in the future.

G. C. Low.

ELIZABETH MACBEAN ROSS, M.B., CH.B. (GLAS.)

Dr. ELIZABETH MACBEAN ROSS, who joined the Society in October, 1913, we regret to announce, died at Kragujevatz, Serbia, on February 14th, 1915, of typhus. Dr. Ross graduated in Glasgow in 1901, taking the degree of M.B. and Ch.B. After practising in London for a short time she went to Persia, where she worked and travelled extensively, often amongst semi-civilized and dangerous tribes. Returning to England in 1914, Dr. Ross studied tropical medicine at the London School of Tropical Medicine, and passed the examination at the termination of the Session. When war broke out she volunteered for service in Serbia, and took charge of the typhus wards at Kragujevatz, but unfortunately she contracted the disease herself

and died after a short illness. At her funeral Colonel Harrison, the British Military Attaché, read the service, and the procession to the cemetery was headed by the band of the Guards of the Crown Prince of Serbia, many Serbians and her colleagues of the Scottish unit being present. Dr. Ross will be much missed by those who knew her, and the Society, by her death, has lost an interesting and energetic personality.

G. C. Low.

Sir RONALD ROSS writes as follows: "I much regret to hear that Dr. ELIZABETH McBEAN ROSS is dead. You ask me to give you an obituary notice of her for the TRANSACTIONS; but I do not possess enough knowledge of her life for this. I have met her only once, last year, on an introduction given to her by Lady St. Helier. But I was very much interested in her and in her very brave travels in Persia. She reminded me very much of Mary Kingsley; and it is a remarkable fact that both these ladies, who shewed such extreme courage in the manner in which they travelled amongst the most barbarous and often savage tribes, should have met their fate by contracting respectively typhoid and typhus in hospitals where they were working during war-time. Miss MACBEAN ROSS (who is no relative of mine) did not, I think, possess quite the personality of Mary Kingsley, but was nevertheless a most remarkable lady, of whom all our countrymen should be proud. I was much struck by the merry manner in which she laughed at the British authorities for being so nervous about her when she was travelling up country in Persia; 'For,' she said 'I never feel so safe as when I am living with brigands.' She was also much interested in tropical medicine.

"Please print this letter if you think it will be of any use as a contributory addition to the obituary notice of her which you propose to publish."

CAPTAIN R. M. C. LINNELL, R.A.M.C.*

A promising career has been recently cut short by the death of Captain R. M. C. LINNELL, R.A.M.C., from cerebro-spinal fever. Dr. LINNELL was educated at Bedford Modern School, St. John's College, Cambridge, and the London Hospital, taking the M.R.C.S.,

L.R.C.P. in 1907. He then became House Physician and House Surgeon at Newport Hospital (Mon.), subsequently taking the Cambridge D.P.H. and the London D.T.M. & H. After a year as Medical Officer at Rossall School, he went out to the Malay States as Medical Officer to the Kuala Lumpur Rubber Co., remaining there from January, 1912, to October, 1914. During this period he made splendid use of the large amount of clinical material at his disposal, paying especial attention to the treatment of malaria in coolies. In October, 1914, he was recalled as an officer of the R.A.M.C. (Special Reserve).

Always an enthusiastic athlete, he was especially successful at long distance running, representing the United Hospitals on several occasions. He also represented his hospital at cricket, and several times captained the team of the Federated Malay States.

C. H. TREADGOLD.

*At the June Meeting of the Society, a very important paper by the late Captain R. M. C. LINNELL, on the "Prophylaxis of Malaria," will be read, and a discussion will take place upon it.—ED.

LIBRARY NOTES.

Under this heading we propose to review recently published works sent us for that purpose, and a short notice of any other works presented to the library.

The Diagnostics and Treatment of Tropical Diseases. E. R. STITT, B.A., M.D.

Readers will remember STITT's little work on *Practical Bacteriology, Blood Work and Animal Parasitology*, and will welcome this second work on the diagnosis and treatment of tropical diseases. Although intended as a companion volume to the former, yet, in order to make it complete in itself, the author has prepared under each disease a paragraph dealing with the laboratory diagnosis of the disease under consideration. This addition will be found useful and will save the student much time and trouble. The work is divided into two parts: Part I. dealing with the different tropical diseases and their treatment; Part II. with diagnosis. Under the first heading the different diseases are sub-divided as follows:—(1) Diseases due to protozoa; (2) Diseases due to bacteria; (3) Diseases due to filterable viruses; (4) Food deficiency diseases; (5) Helminthic infections; (6) Infectious granulomata of the tropics; (7) Tropical skin diseases; (8) Tropical diseases of disputed nature or minor importance. This sub-division is new and seems to be a sensible one. A glance through the pages of the book shews that the author has worked into the space at his disposal a vast amount of work. Recent work is well treated, often, as a matter of fact, to the exclusion of older and better, but this seems to be a common failing of the present day. Very good diagrammatic plates and photographs are scattered through the work, and these should largely help the student in his study of the subject. It is a useful little book, and can be thoroughly recommended.

G. C. L.

TRANSACTIONS
OF THE
SOCIETY OF TROPICAL MEDICINE
AND HYGIENE.

JULY, 1915.

VOLUME VIII. No. 8.

Proceedings of a Meeting of the Society on Friday, June 18th, 1915,

Sir RONALD ROSS, K.C.B., F.R.S., in the Chair.

ANNUAL MEETING.

The Annual Report of the Council and the Treasurer's Report and Statement of Accounts were duly presented at the Meeting, and received and adopted. These will be printed in the forthcoming issue of the Year Book.

The result of the ballot for the offices of President and Vice-President and for the Council, for the ensuing two years, was then declared as follows :—

President :

Dr. F. M. SANDWITH.

Vice-President :

Surgeon-General Sir DAVID BRUCE, C.B., A.M.S.

Council :

Dr. J. M. ATKINSON.

Mr. E. E. AUSTEN, F.Z.S.

Dr. ARTHUR G. BAGSHAW, C.M.G.

Dr. ANDREW BALFOUR, C.M.G.

Fleet-Surgeon P. W. BASSETT-SMITH, C.B., R.N.

Sir JOHN ROSE BRADFORD, K.C.M.G.

Mr. J. CANTLIE.

Major S. LYLE CUMMINS, M.B., R.A.M.C.

Dr. C. W. DANIELS.

Lieut.-Col. H. E. DRAKE-BROCKMAN, I.M.S.

Dr. C. F. HARFORD.

Dr. W. HARTIGAN.

Colonel W. G. KING, C.I.E., I.M.S.

Dr. G. C. LOW.

Professor E. A. MINCHIN.

Dr. H. B. G. NEWHAM.

Professor W. J. R. SIMPSON, C.M.G.

Professor J. W. W. STEPHENS, M.D.

Dr. C. MORLEY WENYON.

Sir RONALD ROSS then welcomed the newly elected President, Dr. F. M. SANDWITH, and invited him to take the Chair. Dr. SANDWITH, in doing so, thanked the Fellows of the Society of Tropical Medicine and Hygiene for the honour they had done him in electing him President.

A paper by the late Dr. R. M. C. LINNELL, "On Malaria on Rubber Estates," was then read.

SOME OBSERVATIONS ON MALARIA ON RUBBER ESTATES.

BY

R. M. C. LINNELL, B.A., M.R.C.S., L.R.C.P., D.P.H., D.T.M. & H.,

Late Medical Officer to the Kuala Lumpur Rubber Co.

The advice generally given to a European starting for the tropics, is, to take so much quinine a day and not to drink too much whisky. The traveller is led to believe that by these means he will escape malaria, or, should he be unlucky enough to contract it, the attack will be no worse than a slight attack of influenza at home.

I gave quinine grs. v. (and more) a day, as a prophylaxis against malaria, to over 2,000 Tamil coolies for two-and-a-half years, and the results were most disappointing; in fact, as soon as the coolies became accustomed to the quinine, it seemed to lose any beneficial effect it had had, and acted almost as a slow poison.

Europeans who have lived in fever districts in the tropics for considerable periods, and kept free from malaria on the daily use of prophylactic quinine, have probably had a special personal immunity against the disease, used their mosquito-rooms, or gone to bed very early, and even then have probably slept in healthy areas.

The following observations on the administration of prophylactic quinine were carried out on Tamil coolies working on rubber estates.

The Tamil coolie is a poor feeder—living chiefly on rice—and he has little or no stamina and will not use mosquito-curtains, so if the district in which he lives is malarial he is practically certain to become infected.

The other imported labour on the rubber estates with which I am connected is Chinese. The Chinaman is a much better feeder, more robust, and uses his mosquito-curtain, and will exist where a Tamil dies.

The Tamil is uneducated, has little control over his inclinations, and will not take quinine of his own free will, and so it has to be administered to him, and this is done at muster either in the morning or afternoon.

The quinine used was the sulphate, chloride and bi-hydrochloride, administered in glycerine capsules and in solution.

I did not find that one sort of quinine, as a prophylactic, gave much better results than another, or that solution was much preferable to the capsule. The coolie did not object to the capsules as much as he did to the solution; his objections to the latter being so marked in some cases, that many of a labour force would abscond, so as to avoid the quinine muster: this would so disorganize the work that the quinine in solution had to be discontinued, unless as a punishment, when it was discovered that some coolie had not swallowed his capsule. The muster is held after the morning or afternoon meal, then at the end of the muster each coolie has his capsule of quinine (under European supervision), and this is washed down with a drink of ac. hyd. dil. or ac. sulph. dil. I gave emetics on several occasions, about an hour afterwards, but was never able to discover the capsule.

On unhealthy estates the morning feed of curry and rice is provided at the estate's expense, so that there is no chance of a coolie going chilled and hungry into the field.

If the quinine is given on an empty stomach the coolie generally vomits, and cannot eat his rice; also, this vomiting often happens with quinine taken after a meal, if given in solution: so, after a meal, the capsule is generally given, and not the solution.

Afternoon musters are more convenient for the administration of quinine, as the coolie has had his chief meal, and, as his work is finished, is more happy than in the cold, early morning. When a coolie is attacked by malaria, he has grs. xxx. quinine, in solution, given to him that day, and is probably sent into hospital that day or the next.

In all cases in hospital the quinine is given in solution.

From Dr. MALCOLM WATSON'S able monograph on *Malaria in the F. M. S.*, it is generally known that flat country can be made healthy by open drains, after having cleared the jungle, but that the malaria is bad where the country is broken, and ravines occur. Here, open drains are much worse than useless—unless concrete inverts are used in some system of sub-soil drainage—and some form of sub-soil drainage has to be employed.

The following observations were made in typically broken country:—

1. There is generally a double seasonal wave in the malaria rate. The first rise synchronises with the first increase in the rainfall, being highest in April—June. The second wave generally just precedes the second increase in the rainfall, and is highest September—October. (*Vide* Charts I. and II.).

As to whether this is due to the increased rainfall or synchronises with it, I have no definite opinion, but possibly it is due to the increased flow of water washing out of the ravines something which keeps the mosquito from becoming infected, because:—

(a) One seems to be able to catch as many (if not more) so-called fever-carrying mosquitoes in the healthy period as in the wet season;

(b) On a healthy estate which I had the chance of watching there was no seasonal wave, with the rainfall or without;

(c) Fever-carrying mosquitoes can be caught in any quantity on this healthy estate, the whole year round, and yet there is practically no fever. This estate was deeply cultivated all over, and this caused no increase of fever;

(d) The increase in malaria does not follow the rainfall in such a way as to give time for a new swarm of mosquitoes to be hatched out and become infected. (*Vide* later).

The first increase of malaria synchronises with the flowering of the rubber trees. The Malays recognise this fact and expect that the fever will not abate until this is over.

I am told by tea-planters that the flowering on certain tea estates synchronises also with an outbreak of fever, but I have had no experience of this. In my opinion, the seasonal wave of malaria on

unhealthy estates cannot be stopped by quinine alone. To do this, some sort of drainage must be attempted. (*Vide* Charts I. and II.).

It will be noticed that these waves were maintained in spite of the daily administration of quinine, and with 63 per cent. and 54 per cent. of the labour force shewing active malaria in some of its months, it did not seem to be much good continuing its use.

Having such disappointing results with the daily use of small doses of quinine, I tried to determine if grs. v. quinine per day would protect new coolies going to live on an intensely malarial site.

2. Twenty-four Tamils were taken, arriving from India. These were the first coolies to reside on an area surrounded by ravines. In these ravines the larvæ of *Nyssorhynchus maculatus* could be found in quantities.

I examined all their bloods and found no parasites nor any mononuclear increase suggesting malaria.

At that time, examining coolies arriving in the F.M.S. for the first time *via* Port Swettenham, I found that about 5 per cent. had parasites in their blood. None of these coolies had been in the F.M.S. previously. They were given grs. v. quinine sulph. daily, followed by a drink of ac. hyd. dil. On the fourteenth day after arrival, five had fever, and their bloods shewed malignant malarial parasites. I found no parasites in the bloods of the others. Evidently quinine grs. v. in an intensely malarial area was not enough to prevent malaria.

3. Then, to ascertain if a better effect could be caused by increasing the daily dose, I took another very unhealthy area (death rate, 1913, 111·0 per mille). These coolies had had grs. v. daily, with the above watched result, so I increased the quinine, viz.:—

Amount of Quinine Daily.	Period.	Average Labour Force.	Percentage Sick Daily.
Quin. sulph. grs. x.	6 months	24	15·7
„ grs. xv.	5 „	30	19·7
„ grs. xx.	5 „	25	19·5

I examined the bloods of these coolies from time to time and found that practically all the sickness was due to malaria; but, examining all the bloods at the end of these sixteen months, I found malarial parasites in 25 per cent. Perchance, if I had examined the bloods, say, on

three consecutive days, I should have found the percentage to be much higher.

Probably these coolies developed a quinine-fast parasite, as when they came into hospital on a healthy site, recurrences were extremely common on big doses of quinine (grs. xlv. per day). The area became uninhabitable and so the coolies were moved two miles away, into a healthy Chinese village, but recurrences are still very numerous, in spite of the continued use of quinine, and it seems that it will be necessary to replace this effete crowd by a more robust lot.

These two observations were carried out on very small numbers of coolies, as a larger force could not have existed there.

In order to determine whether the continued use of quin. grs. v. per day was of any prophylactic use, I carried out some observations on the coolies of another unhealthy area. There was some discussion as to the advisability of moving these lines, but as no healthy area could be guaranteed, except at an inconvenient distance, this was not done.

The death-rate in 1912 was 71·4 per mille, and as many as 63 per cent. and 54 per cent. of the labour force of 180 shewed clinical malaria in some of the unhealthy months. (*Vide* Chart I.).

The coolie-lines consisted of three blocks, steel "jack-roofed" lines with cement floors, 50 feet apart and about 100 yards from a river, with secondary jungle and many ravines on the other side of the river.

The larvæ of the following anopheline mosquitoes were found in the swamp and ravines (and the adults were often found in the lines).

Nyssomyzomyia rosi.

Myzorhynchus sinensis.

Myzomyia albirostris.

Nyssorhynchus maculatus.

Nyssorhynchus fuliginosus.

The spleen-rate was 93·7 per cent. (32 children examined who had been more than six months on the estate).

Ankylostome ova in fæces, 22·7 per cent. (123 examined).

Blood examinations (162 examined)—Positive, 46·29 per cent.

Negative, 53·70 per cent.

Positive Bloods—Malignant, 74·66 per cent.

Benign Tertian, 20·00 per cent.

Quartan, 2·66 per cent.

The 180 coolies were divided into two lots and mustered each day separately, the Manager, Mr. C. St. John Wright, kindly maintaining the numbers as nearly equal as possible. Each lot was fed, at the estate's expense, with hot curry and rice in the early morning.

Lot A. was given a decoction of coriander seeds, instead of the quin. sulph. grs. v., washed down with a drink of ac. hyd. dil., which was given to Lot. B.

Any coolie in either A or B had grs. xxx. quin., in solution, during the day on which he shewed clinical malaria. The coriander decoction was used, as the coolies have faith in its prophylactic qualities, and the lot *not* having quinine had to have something, so that no jealousies should arise.

The individuals who shewed malaria were counted each week, commencing afresh the next week. The first observation was carried on for eight weeks.

		A. (90 Coolies.)		B. (90 Coolies.)	
		Coriander Decoction.		Quinine grs. v. daily.	
		Sick	Clinical	Sick	Clinical
		(all causes).	Malaria.	(all causes).	Malaria.
1st week	...	25	9	57	27
2nd	„ ...	34	22	57	26
3rd	„ ...	41	22	44	14
4th	„ ...	39	21	47	17
5th	„ ...	28	16	29	15
6th	„ ...	33	17	39	30
7th	„ ...	32	14	42	20
8th	„ ...	22	10	27	15
		<hr/>	<hr/>	<hr/>	<hr/>
		254	131	342	164
		<hr/>	<hr/>	<hr/>	<hr/>

All these coolies had been having quinine daily for over two years; the most marked benefit seemed to be during the first week, that is, when they ceased taking their daily prophylactic quinine.

The coolies were then changed over for another eight weeks.

B. (90 Coolies.)				A. (90 Coolies.)			
Coriander Decoction.				Quinine grs. v. daily.			
		Sick	Clinical			Sick	Clinical
		(all causes.)	Malaria.			(all causes.)	Malaria.
1st week	...	35	20			39	12
2nd "	...	24	10			33	16
3rd "	...	21	10			31	15
4th "	...	26	14			25	12
5th "	...	27	10			26	11
6th "	...	21	10			21	15
7th "	...	27	14			27	11
8th "	...	19	8			29	17
		<hr/>	<hr/>			<hr/>	<hr/>
		200	96			241	109
		<hr/>	<hr/>			<hr/>	<hr/>

In either case, the coolies who were *not* having quinine daily were healthier than those who were.

During this second observation the jungle across the river was opened up, and a marked reduction in the number of malaria cases occurred.

The lots were then changed over for a fortnight, the number of coolies being maintained the same (approximately).

A. Coriander.				B. Quinine grs. v.			
		Sick	Clinical			Sick	Clinical
		(all causes.)	Malaria.			(all causes.)	Malaria.
1st week	...	25	11			28	12
2nd "	...	28	10			24	11
		<hr/>	<hr/>			<hr/>	<hr/>
		53	21			52	23
		<hr/>	<hr/>			<hr/>	<hr/>

Changed over for another fortnight.

B. Coriander.				A. Quinine grs. v.			
		Sick	Clinical			Sick	Clinical
		(all causes.)	Malaria.			(all causes.)	Malaria.
1st week	...	22	7			23	7
2nd "	...	16	4			28	6
		<hr/>	<hr/>			<hr/>	<hr/>
		38	11			51	13
		<hr/>	<hr/>			<hr/>	<hr/>

Changed over for three weeks.

		A. Coriander.		B. Quinine grs. v.	
		Sick	Clinical	Sick	Clinical
		(all causes).	Malaria.	(all causes).	Malaria.
1st week	...	28	7	19	7
2nd	„	14	5	25	6
3rd	„	25	10	25	10
		<hr/> 67	<hr/> 22	<hr/> 69	<hr/> 23

The quinine and decoction of coriander were administered under European supervision (Mr. H. L. Linnell, Assistant-in-Charge of the Division) and an experienced dresser was put in sole charge of the lines, so that every coolie coming in from the field with fever could be accounted for and properly treated. It was impossible to examine the blood of every patient, but the greater number were examined. There was little difficulty with the diagnosis, the type of fever being well marked.

In each observation the non-administration of daily prophylactic quinine gave better results than quinine administered daily.

The next observation was in order to see whether the coriander was of any prophylactic use.

Lot A was given no prophylactic medicine, while B was given decoction of coriander. In either lot when a coolie shewed clinical malaria he had grs. xxx. quinine in solution on that day. This had to be done as the coolies would otherwise in all probability have died.

The first observation lasted nineteen days, and these are the figures:—

A. No prophylactic.		B. Coriander.	
Total sick	Clinical	Total sick	Clinical
(all causes).	Malaria.	(all causes).	Malaria.
47	18	59	18

The site having become much healthier, an alteration in the labour force of the estate then occurred, and a new batch of coolies was brought into the line and some of the old coolies moved elsewhere, so the experiment was discontinued until these had time to settle down. The old coolies were then mustered again separately, and the observation continued for seventeen days.

A. (No prophylaxis).		B. (Decoct. Coriander).	
Number of coolies 65		Number of coolies 76	
Total sick (all causes).	Clinical Malaria.	Total sick (all causes).	Clinical Malaria.
61	13 (20 per cent.)	41	12 (15·7 per cent.)

A Tamil feast then occupied two days, but after this the observation was continued for another seventeen days.

A. (No prophylaxis).		B. (Decoct. Coriander).	
Number of coolies 66		Number of coolies 69	
Total sick.	Clinical Malaria.	Total sick.	Clinical Malaria.
34	9 (13·6 per cent.)	58	13 (18·8 per cent.)

The coolies were then changed over for eighteen days.

A. (Decoct. Coriander).		B. (No prophylaxis).	
Number of coolies 56		Number of coolies 57	
Total sick.	Clinical Malaria.	Total sick.	Clinical Malaria.
34	7	24	7

(*Note.*—These last observations were carried out during the most healthy period of the year, that is, just before the first increase in the rainfall).

When I tried decoction of coriander on patients in hospital, I found that in many patients the parasites disappeared, but the same thing often happened when the patient was put to rest and given some ordinary treatment (*not* quinine.)

Probably the coriander does have some effect on the malarial parasite. It makes a very palatable alternative to prophylactic quinine, and so this is still given in the lines to the coolies, alternating it with quinine as a prophylaxis, and in hospital, instead of tea, they drink three "baths" of coriander, as they have great faith in it.

The first seasonal increase in the rainfall being now due, and with it an increase in the number of cases of malaria on two estates, I put the coolies on quinine grs. v. daily for a week, and then coriander decoction for a week, with marked beneficial results.

In the same malaria season of the previous year the coolies had had grs. v. and grs. x. with no result, in fact there were six deaths on one estate of coolies who had a hot feed of rice and curry in the early morning, and after it their quinine. These coolies were seemingly fit and well, yet, in spite of intravenous injections of quinine, intramuscular injections, etc., they were dead before evening, and on examining their bloods, I found them to be teeming with malarial parasites. Now, however, in the season just come, malaria has been

of much decreased intensity, and up to the time of writing (nine months) there has been no case of cerebral malaria. I do not think that this is due to a general wave of less intensity, as the estates in the vicinity have had a worse wave than usual. On another estate there are two sets of lines about two miles apart; each set is surrounded by ravines, and in these ravines the larvæ of *maculatus* can be found in quantities.

Lines A were unprotected by sub-soil drainage.

B were all but protected.

			Average Labour force.	Percentage sick per day.
Aug., 1913	A B	Quin. grs. v. daily.	257 92	13·80 9·70
Sept., "	A B		257 88	15·00 4·50
Oct., "	A B		239 82	14·20 4·20
Nov., "	A B		232 70	20·60 8·50
Dec., "	A B		209 62	25·00 14·00
Jan., 1914	A B	A—Quin. grs. v. and coriander decoct. alternate weeks. B—Quin. grs. v. daily.	170 74	12·90 12·80
Feb., "	A B		168 93	11·30 16·90
Mar., "	A B		165 89	8·10 13·00
April, 1914	A B		164 76	9·10 8·00
May, "	A B	A & B—Quin. grs. v. & decoct. coriander alternate weeks.	164 100	10·51 6·11
June, "	A B		174 80	10·60 8·30
July, "	A B		180 112	11·54 4·98
Aug., "	A B		159 113	10·59 7·05
Sept., "	A B		152 87	9·60 10·10

Both lots were given quinine grs. v. daily, and B was always healthier than A. At the end of six months' observation, A was given quinine grs. v. daily and coriander in alternate weeks, whilst B was kept on with its daily grs. v. quinine. Immediately A became healthier than B.

In whatever way the changes were rung here, every time the batch of coolies taking quinine grs. v. daily for a longer period than a fortnight were unhealthier than the lot taking quinine in alternate weeks. The result was the more marked as the number of coolies in B was only about half that in A.

(Note.—As a general rule a small lot of coolies will be healthier than a large lot, on an unhealthy area).

It is hard to get records of any number of Europeans and the results in their case of quinine prophylaxis, but when I left England I was advised to take quinine grs. v. daily. I did from my arrival at Penang and took the bi-hydrochloride most religiously until I had my first attack of malaria (three months after arrival in the tropics).

Having followed the ordinary routine treatment I continued with my prophylactic grs. v. daily and grs. x. once a week until I got my second attack. Then I thought fit to take it "when I wanted it" and had no more attacks (during fifteen months).

The following is a malarial history of the Europeans living in two bungalows, one hundred yards apart, on a very unhealthy area.

"G" arrived in the tropics for the first time since a baby (in West Indies when one year old); took quinine bi-sulph. grs. v. daily. In three weeks had malignant malaria and blackwater fever. He had ordinary routine treatment and then dropped to grs. x daily. Had recurring attacks and so always took either grs. x. or grs. xx. every day. His spleen became enlarged and after a year he had to go to another place, fairly healthy, where he stopped his quinine and became quite healthy. He thought the risk too great to stop his quinine whilst living in the unhealthy area.

"S.," in the same bungalow, malignant fever constantly in spite of quinine grs. x. daily. . . He had to leave for another estate.

"Baron C.," same bungalow, quinine grs. v. daily and grs. x. on Sundays. No fever for six months, then malignant malaria which lasted thirteen days while on quinine bi-hyd. grs. xxx., in solution.

The lots were then changed over.

B. (100 Coolies).				A. (121 Coolies).	
Quin. grs. v. and Decoct. Coriander alternate weeks.				Grs. x. (sixth and seventh days).	
	Total sick.	Clinical Malaria.		Total sick.	Clinical Malaria.
1st week ...	31	13		36	15
2nd „ ...	20	10		40	11
3rd „ ...	19	8		40	12
4th „ ...	20	12		48	18
5th „ ...	24	9		50	12
6th „ ...	24	7		43	10
7th „ ...	19	5		30	10
	<hr/>	<hr/>		<hr/>	<hr/>
	157	64		287	88 (72·7 %)
	<hr/>	<hr/>		<hr/>	<hr/>

The greater benefit seems to be with the grs. v. and decoct. coriander, given alternate weeks.

This observation could not be carried further, as war broke out and I was called home.

There is another point which is of interest.

I kept careful records of the rainfall, and with it the percentage of coolies shewing active clinical malaria. The increase of the malaria does not seem to follow the accepted rule, *i.e.*, time for the eggs to hatch, the development of the mosquito, and an incubation period after infection, etc. The increase in the malaria rate seems to occur during “next week but one” following a low weekly rainfall, but this is more clearly appreciated in actual practice than through a study of figures. (Of course, if the coolies get caught in the rain and get chilled, this brings out an attack of fever, so, to obviate this to some extent, there are shelter sheds on every division into which the coolies can go when it begins to rain.)

W—N ESTATE.

K—G ESTATE.

Date week ending.	Lab. force.	Per-centage sick per day.	Per-centage Mal. per wk.	Rain fall.	Quin. per day.	Lab. force.	Per-centage sick per day.	Per-centage Mal. per wk.	Rain fall.	Prophylaxis.
June 6	417	8·87	2·63	1·20	Grs. x.	234	8·96	6·83	1·45	Grs. v.
„ 13	420	7·48	2·38	6·68	Nil.	232	10·40	7·32	9·04	Coriander.
„ 20	431	7·32	6·03	4·05	Grs. x.	228	6·45	6·57	0·58	Grs. v.
„ 27	436	7·20	5·27	Nil.	Nil.	225	6·78	5·77	0·21	Coriander.
July 4	429	7·74	2·79	1·27	Grs. x.	215	8·03	11·16	1·46	$\left\{ \begin{array}{l} \frac{1}{2} \text{ Quin. grs. v.} \\ \frac{1}{2} \text{ Decoct. cor.} \end{array} \right.$
„ 11	427	9·35	8·66	0·45	Nil.	212	8·89	8·49	0·65	„ „
„ 18	406	11·08	4·18	1·60	Grs. x.	211	7·78	10·90	1·16	„ „
„ 25	414	7·03	4·10	Nil.	Nil.	207	6·89	8·69	Nil.	„ „
Aug. 1	413	6·52	3·38	0·30	Grs. x.	206	8·38	9·22	Nil.	„ „
„ 8	403	9·92	8·43	0·50	Nil.	204	10·55	9·31	3·07	„ „
„ 15	420	10·16	5·47	1·75	Grs. x.	218	8·12	12·38	2·35	„ „
„ 22	268	13·37	4·85	2·79	Nil.	224	8·41	12·49	1·70	„ „
„ 29	277	12·78	6·85	Nil.	Grs. x.	220	10·06	9·54	Nil.	„ „
Sept. 5	278	11·65	5·03	1·83	Nil.	219	8·60	9·13	2·68	„ „
„ 12	276	14·69	9·78	1·11	Grs. x.	220	13·63	2·43	Nil.	„ „

NOTE.—During the week ending August 22nd many coolies were moved to a new lot of lines.

NOTE.—After week ending June 27th half coolies continued quinine and coriander alternate weeks—whilst half had quinine grs. x. every sixth and seventh day.

I have figures complete for many months, but the above shew the run of the malaria. If the increase is coming it does not seem to matter much if quinine is given or not, but quinine administered in alternate weeks seems to lessen its intensity considerably—shewn by the absence of cerebral and other bad symptoms.

It is an interesting fact that, in spite of all the quinine given to these coolies, and in spite of the out-of-proportion number of cerebral cases, I never had a case of blackwater fever on these two estates.

W—n Estate like K—g Estate is an old estate, and the coolies come and go from India as they please. W—n coolies are more

anæmic than the K—g coolies, although the lines are only about two miles apart. This is probably due to the amount of ankylostomiasis combined with the malaria. W—n (spleen rate, 75 per cent.) shews an ankylostome rate of 41·2 per cent. (339 examined), whilst K—g (spleen rate, 93 per cent.) shews one of 22·7 per cent. (123 examined).

The malaria figures for W—n and K—g are as follows:—

W—N ESTATE.				K—G ESTATE.			
Number examined		... 736		Number examined		... 162	
Positive	52·03%	Positive	46·29%
Negative	47·07%	Negative	53·71%
<i>Positive Bloods—</i>				<i>Positive Bloods—</i>			
Malignant	75·97%	Malignant	74·66%
Benign tertian	16·18%	Benign tertian	20·00%
Quartan	2·61%	Quartan	2·66%
Benign and Malignant			4·77%	Benign and Malignant			1·33%
Quartan and Malignant			·78%	Quartan and Malignant			Nil.
Benign and Quartan			·26%	Benign and Quartan			1·33%

On another estate (K—t), which is quite healthy, there is only about 1 per cent. malaria per month and a death-rate of 10 per mille; the ankylostome rate is about the same as that of W—n. Yet it is extremely rare to admit into hospital a patient for ankylostomiasis.

Following the history of malarial patients into hospital, one is struck by the tremendous number of cases which recur whilst on large doses of quinine. The routine treatment in the Kent Central Hospital is as follows:—

On admission the malarial patient has a large dose of mist. alba, and is put on milk and sol. quin., grs. xv. t.d.s. Next day the patient has ankylostome treatment with oleum chenopodium, \mathfrak{m} vii., at 6 a.m., 7 a.m. and 8 a.m., administered in a glycerine capsule (being allowed no solid food). Then at 11 a.m. he has an aperient.

I learnt this treatment for ankylostomiasis at Dr. SCHÜFFNER'S Hospital in Sumatra, and, in my experience, it is much more efficacious than thymol-beta-naphthol or eucalyptus. There seems to be no danger and it clears out all sorts of worms.

I did have two patients (among some thousands) who had albumin in their urine on the day after treatment, but they were very anæmic, and

so probably the *ol. chenop.* was not the cause. I reported these cases to Professor SCHÜFFNER, and he stated that he had not seen it in any of the large number of cases he had treated.

(*Note.*—Ankylostomiasis is very debilitating in Sumatra, and all the coolies have to attend hospital every six months for a microscopic examination of their *fæces*; by this means chiefly the death-rate on the estates is kept at about 10 per mille. The treatment by *ol. chenop.* has replaced the other ankylostome treatments there).

As regards round worms, sometimes when a child passes a large number of worms (one child aged six passed 452) the child may die the same night whilst asleep; the child is very anæmic, say 10 per cent. hæmaglobin Tallquist or less, so probably he is very susceptible to any toxin absorbed by the worms.

If, on admission, the malaria is very intense, and the patient is comatose or very much collapsed, in addition to strychnine, brandy, etc., the quinine is given by the mouth, it is my experience that injections of quinine are practically useless. I have given intravenous and intramuscular injections with little success. It may be that the coolies were saturated with quinine beforehand, but the only way of saving these cases seems to be "by mouth," and to give plenty.

If the patient can swallow, he is given an ounce of salts and quin. bi-hyd. in solution, grs. xx. four or five times during the day.

If the patient is comatose and cannot swallow, which is often the case, the stomach is washed out, the salts are given, and the same amount of quinine given through a nasal tube.

Whilst with injections I lost the greater number of cases, by this means it became extremely rare to lose a case at all.

One intramuscular dose may be given, but this is generally for the sake of the relatives, and for the little absorbed to carry on, when the oral doses have done their work.

With ordinary cases, the routine is to give grs. xv. t.d.s. in solution. This, unless combined with bromide, makes the coolie so dizzy that he will often fall off his bed. But, in spite of this, the recurrences are extremely common, and these generally occur about the tenth day. I examined the bloods of 150 cases every day and found that if there was no temperature yet parasites could generally be found, or possibly there was a temperature and no parasites about this date.

These recurrences became so marked that a rule had to be made that every patient should remain in hospital at least eleven days, and that the bloods of all patients should be examined on the ninth, tenth and eleventh days, and if a patient shewed parasites or fever during those days, he should remain in hospital another ten days. A patient only returned on the next tenth day if this was not done.

As so many recurred about the tenth day on quin. grs. xv. t.d.s., it seemed useless to continue administering the quinine to recurring malarial cases, so I then tried neo-salvarsan (4 grs. in 10 cc. distilled water—given intravenously) and was successful with it, when given about the sixth to eighth day after the appearance of parasites or fever. I did not get good results when giving it on the day of fever, or appearance of parasites.

E.g., Meenatchey (Tamil). On admission, malignant. Quin. grs. xv. t.d.s.

24th day	...	Fever (malignant) (injection neo-salvarsan).
23rd „	...	Fever (benign).
40th „	...	Malignant.
41st „	...	Crescents.
42nd „	...	Crescents in morning, fever and benign tert. in evening.
48th „	...	Neo-salvarsan. Benign and malignant.
56th „	...	Fever and malignant.
63rd „	...	Neo-salvarsan.
63rd to 93rd day		No fever or parasites.

Kathaye (Tamil). Admission temperature 100·4. No parasites.
Aged 42. Quin. grs. xv. t.d.s.

6th day	...	Fever and malignant.
16th „	...	Fever and malignant.
27th „	...	Fever—no parasites.
36th & 37th day		Fever and malignant.
45th day	...	Fever—no parasites.
50th „	...	Neo-salvarsan.
50th to 80th day		No fever or parasites.

Porzhy (Tamil). On admission temperature normal. Aged 3. Spleen to mid-line, $1\frac{1}{2}$ inch umbilicus. Ol. chenopodium and hæm. 5 per cent. (Tallquist). Quin. grs. v. t.d.s. Benign tertian—round worms.

12th day	...	Fever and benign.
20th „	...	Fever and malignant.
23rd to 25th day		Fever—no parasites.
33rd day	...	Fever (malignant).
47th „	...	Fever—no parasites.
54th „	...	Neo-salvarsan (0·2 grs.).
54th to 84th day		No fever or parasites.

For some reason quinine does not seem to be of much effect when the parasites are not in the peripheral blood. It seems to be well recognised that they “lie up” in the spleen, etc.

E.g., Alagappon (Tamil). Aged 17. On admission, temperature 98·8. Spleen 2 inches from umbilicus. No parasites in blood or fæces. Hæm. 45 per cent. (Tallquist). Treatment, quin. grs. xv. t.d.s.

10th day	...	Fever—no parasites.
16th „	...	Fever (malignant).
18th „	...	Fever (malignant).
32nd „	...	Fever—no parasites.

Hæm. 20 per cent., œdema of legs.

As patient appeared to be doing badly, I thought that the parasites in the spleen should be disturbed if possible, and as the patient looked as if he would die in spite of any treatment, I thought it justifiable to inject grs. xv. bi. hyd. (sol.) directly into the spleen. Patient suffered from dyspnœa and complained of a little pain on the next day—23rd day—patient had no fever, but his blood teemed with malignant “rings.” One of the heaviest infections I have ever seen.

33rd to 39th day		Splenic rub—on palpating spleen.
41st day	...	Fever—no parasites.
46th „	...	Neo-salvarsan. (Hæm. 25 per cent.).
62nd „	...	Hæm. 45 per cent.
74th „	...	Discharged. (Hæm. 55 per cent.)

Note.—No parasites or fever after 46th day.

I gave many intravenous injections of neo-salvarsan, and whenever it was given between the sixth and eighth days after the appearance of parasites or fever, great benefit followed. In all cases the quinine was continued, and so whether it was the neo-salvarsan so acting on the parasite that the quinine could finish it off, or the neo-salvarsan acting by itself, I give no opinion.

Whenever the neo-salvarsan was given on any other days than those mentioned, its action was most uncertain, and when given on the day when the parasites or fever were due, it seemed to be useless.

When given whilst "crescents" were in the blood, it seemed to have little effect on their disappearance. The "crescents" persisted, but they seemed to be harmless, and watching these cases up to fifty days, there seemed to be no recurrences of fever.

Malarial spleens.—The Chinese seem to have known for a long time that pineapples are very efficacious for getting rid of oedema (in their case, generally due to beriberi), and as one of the best treatments for beriberi seems to be a diet of fresh vegetables and no salt, I thought that I would try pineapples on malarial patients. I did not find that the pineapples had any effect on the parasite, but that they did have a marked effect in reducing the size of malarial spleens.

E.g., Periasomy (Tamil). Aged 32. On admission, temperature 99·8. Malignant parasites. Spleen 8 inches below ribs. Quinine for 4 days and then stopped and put on pineapples.

4th day	...	Fever and parasites.
6th "	...	Fever and parasites.
15th "	...	Fever.
17th "	...	Fever.
19th "	...	Fever and parasites.
25th "	...	Fever and parasites.
26th "	...	Parasites.
27th "	...	Parasites.
28th "	...	Fever and parasites.
29th to 35th day		Parasites.
44th day	...	Spleen 4 inches below ribs.
45th "	...	Spleen 3 inches below ribs.
46th "	...	Spleen and parasites.

50th day	...	Fever.
51st „	...	Spleen 1 inch.
54th „	...	Fever.
64th „	...	Spleen $\frac{1}{2}$ inch.
67th „	...	No spleen.

It is to be noted that the reduction in the size of the spleen took place in spite of the patient having *no* quinine and in spite of the recurring attacks of malaria.

Periasomy was discharged from hospital September 1st, and was re-admitted October 20th with pneumonia, when his spleen was just as large as before. However, the spleen was reduced, this time in 48 days. He stated that he had had no fever whilst out of hospital (he was not off work), and I had seen him about a fortnight before his re-admittance. He had no palpable spleen then so the spleen must have enlarged very rapidly.

Some enlarged spleens reduce very easily. These are cases where the coolie had not been very long in a malarial district.

E.g., Palaniondy (Tamil). Aged 30. In F.M.S. $1\frac{1}{2}$ years. Did not complain of fever until 3 months previous to admittance to hospital. On admission, temperature 99.6. Benign tert. Spleen 6 inches below ribs.

Treatment: Pineapple and quinine grs. x. t.d.s.

No spleen felt in 11 days.

In other cases where the patient has lived on malarial sites for some years, pineapples seem to have little effect, except to make the spleen firmer and easily movable and to raise the hæmoglobin index of the patient.

Annamalai (Tamil). Aged 27. On unhealthy estate for some years. In hospital many times with fever. On admission, spleen 2 inches to right of mid-line. 2 inches below umbilicus. (Edema of legs. Hæm. 25 per cent. (Tallquist). No parasites found. Treatment: ol. chenopodium, pineapples and quinine.

18th day	...	Fever—no parasites.
21st „	...	Spleen 1 inch right of umbilicus. 1 inch below umbilicus.
31st „	...	Spleen mid-line and at umbilicus.
34th „	...	Hæm. 30 per cent.

52nd day	...	Spleen 2 fingers from umbilicus.
63rd „	...	Fever—no parasites.
67th „	...	Hæm. 60 per cent.
76th „	...	Spleen mid-line 2 fingers from umbilicus.
83rd „	...	Spleen $1\frac{1}{2}$ inches left of mid-line. $2\frac{1}{2}$ inches from umbilicus, very movable.
85th „	...	Hæm. 70 per cent. Discharged.

Sometimes it seems as if the complete reduction of a malarial spleen is of no benefit to the patient, if he be sent to reside on an intensely malarial site.

Many patients complain that whilst they had a big spleen, they did have fever, but it did not hurt them and they could work. Then when the spleen had gone, they were better for a time and then they got much worse fever than they had before.

Karuppiah (Tamil). Aged 12. No parasites. Spleen $7\frac{1}{2}$ inches below ribs. Hæm. 50 per cent. (Tallquist). Treatment: quinine and pineapples. In 17 days, no spleen felt. Hæm. 70 per cent.

This patient was discharged and re-admitted 3 days later suffering from cerebral malaria, benign tertian. Spleen $4\frac{1}{2}$ inches below rib. Patient died next day in spite of intravenous and intramuscular injections of quinine.

I found that the pineapples which gave the best results were the Mauritius variety, not quite ripe. These were given in the early morning and also after meals, one to two a day being eaten by each patient.

When pineapples are to be had at a reasonable price these are given to every patient as part of their diet, as they seem to raise the hæmoglobin indices of anæmic patients much more quickly than iron tonics, besides having an effect on the spleen.

A pineapple garden has now been planted, near the Central Hospital, so that a constant supply of these fruits can be obtained all the year round. I was surprised at the variations in the size of the spleen during different parts of the day, so 31 malarial spleens were measured every four hours for 24 days, from fixed points (1) umbilicus, (2) xiphisternal notch, (3) vertical line drawn from a horizontal line at height of xiphisternal notch to lower end of spleen, (4) a point on

a rib. These points had to be taken, as the spleen enlarges and reduces in such various directions. These measurements were carried on by night as well as day for one week.

I found that the spleen is largest from 8 a.m. to 10 a.m. and again about 6 p.m. to 8 p.m.

These differences in the size of the spleen are not appreciable by ordinary tape-measuring methods until the spleen has lost its flabbiness. As the spleen becomes firmer and freely movable these differences in size can be recognised, some large spleens seemingly diminishing or increasing quite an inch in every direction.

I tried papyrias but I did not find that they had any effect on the size of the spleen, nor had they much effect in raising the hæmoglobin index.

In my opinion these daily variations in size are not due to food, as I kept many patients on milk and castor-oil, and the variation in size took place just the same. I could not take the blood pressure of these patients as I had no machine, but there did not seem to be a synchronous rise and fall in the temperature and pulse rate.

These variations are probably physiological.

Having watched so many recurrences of fever with parasites whilst the patients were on quinine, I thought that it might be possible to give prophylactic quinine so as to prevent these attacks, and so I tabulated the days the coolies were off work with clinical malaria. The days on which the recurrences occur are taken in lots of three days each.

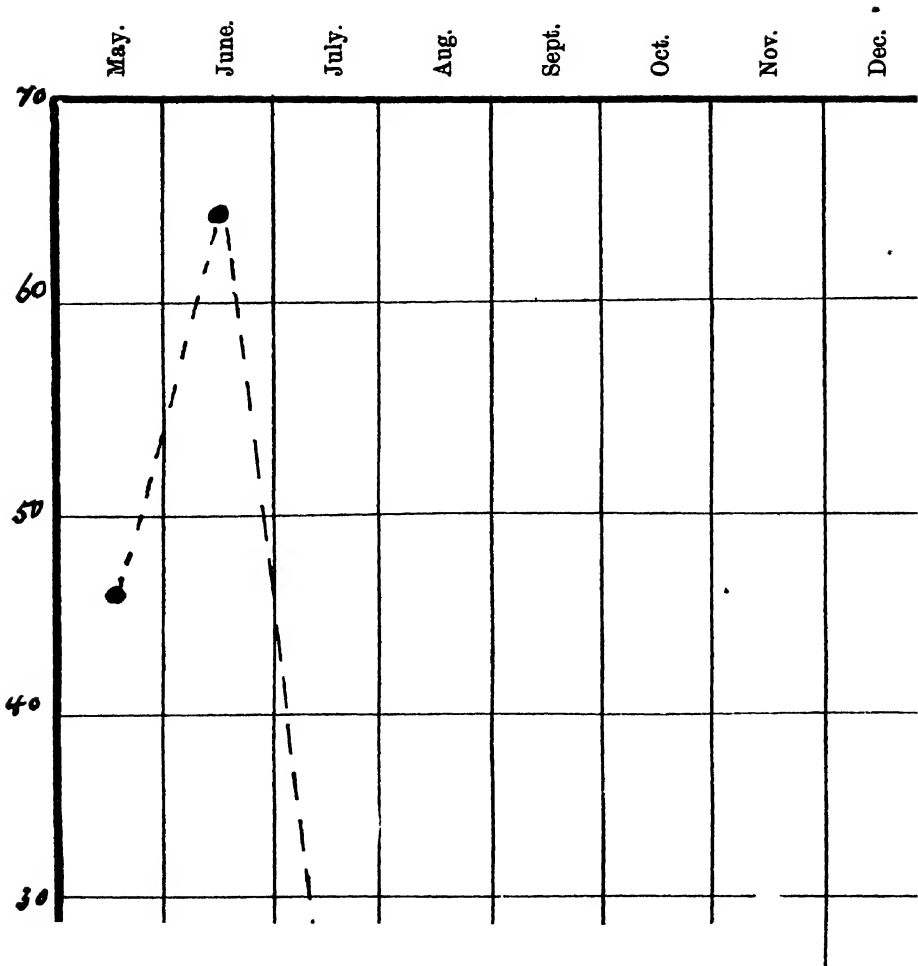
The vertical figures are the percentages of "events" recurring on these lots of three days each. *Vide* charts.

Calculating the number of days, up to 30 days, for the years 1910 and 1911, the average number of days between the recurrences was in 1910, 15·56 days, and in 1911, 15·47 days. In these years the coolies had no prophylactic quinine.

In 1912 the coolies had prophylactic quinine daily and the average time between the recurrences was 15·71 days. In 1913 the coolies continued their daily prophylactic quinine and the time was shortened to 14·56 days, the worst result recorded.

In 1914 the coolies had quinine daily for alternate weeks, and the time between the recurrences was lengthened to 16·71 days, the best result

1912 (No. of Coolies, 209).



These charts do not seem to demonstrate tenth day recurrences to any marked extent. This is probably due to the difference in environment of the coolie. The tenth day recurrences are most marked when the patient is in hospital, that is, on a healthy site, made to sleep in mosquito curtains and doing no hard work. So probably the marked tenth day recurrences are due to well-established infections.

These last five charts are worked out on coolies in full work, and so fatigue, getting wet, constipation, etc., may have predisposed to an attack of malaria. Again, the parasites must have been in the blood many times without the patient exhibiting fever, as, since I have known these coolies (three years) the spleen rate has been about 75 per cent., yet the highest percentage of coolies shewing recurrences was 34·07 per cent. (1914). So about 40 per cent. must have had parasites in the blood and yet not exhibited active fever.

The conclusions I arrived at, after just on three years' observations, were :—

I. Quinine grs. v. daily will not stop an attack of malaria, if the patient lives in an unhealthy area.

II. No amount of quinine on which the coolie can do his work will stop the seasonal wave in ravine country. The area must be sub-soil drained to do this.

III. Interrupted administrations of quinine will do much to prevent the malaria taking a serious form.

IV. In severe cases of malaria (cerebral cases) the best treatment is to wash out the stomach and give quinine, in plenty, by the mouth.

V. The best treatment for recurring cases of malaria is intravenous injections of neo-salvarsan, on the sixth to eighth days following the appearance of parasites or fever, followed by quinine.

VI. Pineapples have an effect in reducing malarial spleens and also raise the hæmoglobin, index. Quinine and pineapples should be given together.

VII. *Oleum chenopodium* is the most efficient vermifuge for removing ankylostome worms. When ankylostomiasis is uncomplicated with malaria, it does not seem to be very debilitating in Selangor.

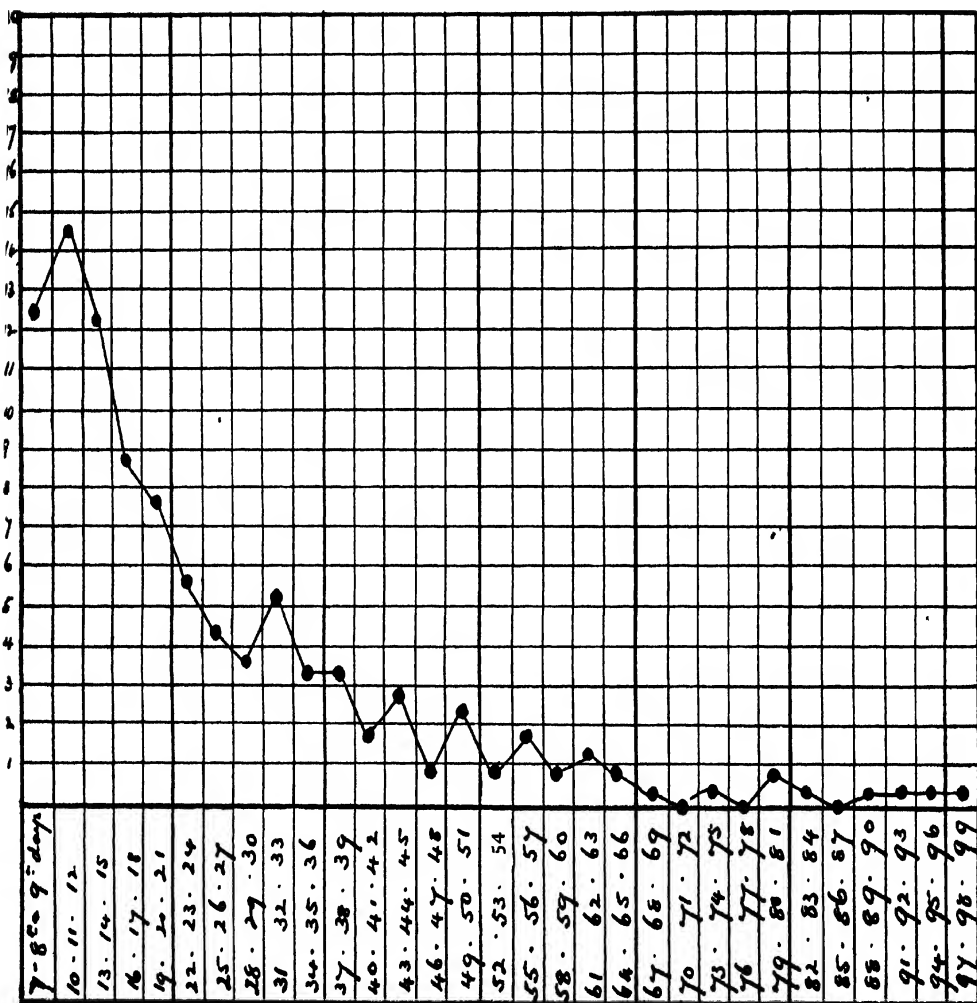
My best thanks are due to Mr. E. B. Skinner, Agent for the Société des Caoutchoucs (F.M.S.), to Mr. H. Armstrong, General Manager, Kuala Lumpur Rubber Co., and all the managers and assistants who gave me every help and assistance in their power to make these observations.

CHART No. 3.

MALARIA ON RUBBER ESTATES. 1910.

No Prophylactic Quinine.

Number of Cases, 699. Number of Cases recurring, 170 (24.32%). Number of recurrences, 248.



MALARIA ON RUBBER ESTATES. 1911.

No Prophylactic Quinine.

Number of Cases, 1,035. Number of Cases recurring, 202 (19.51%). Number of recurrences, 280.

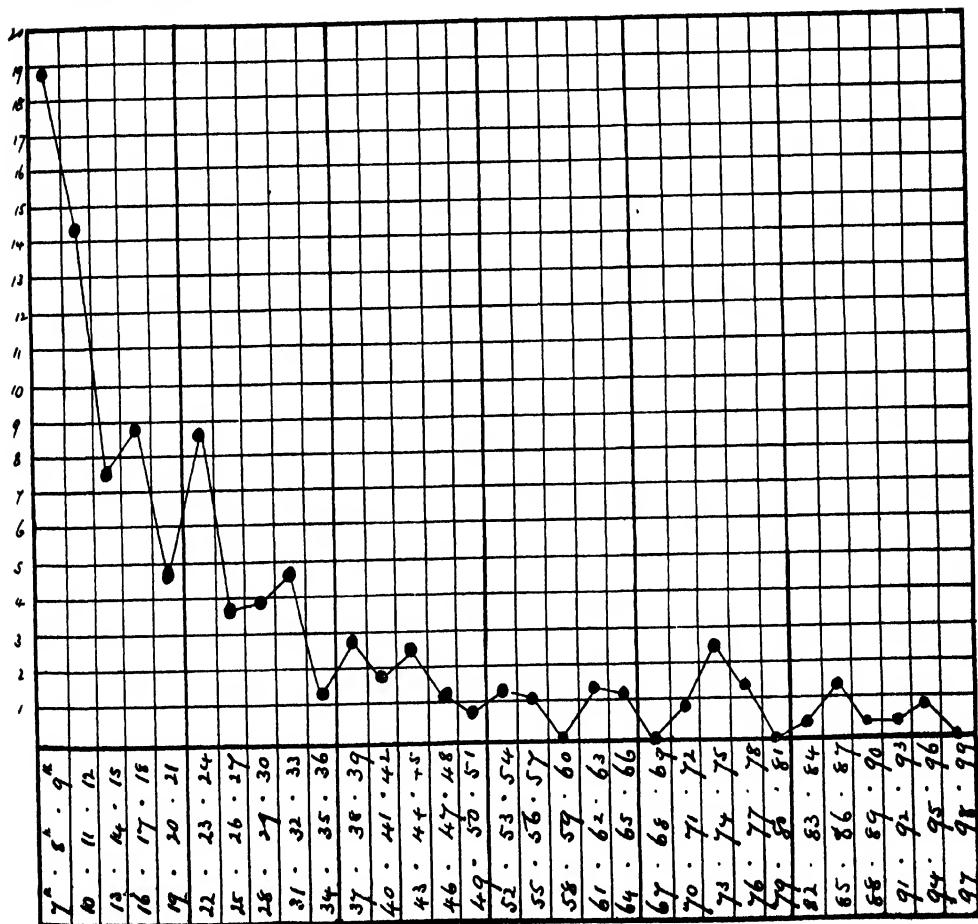
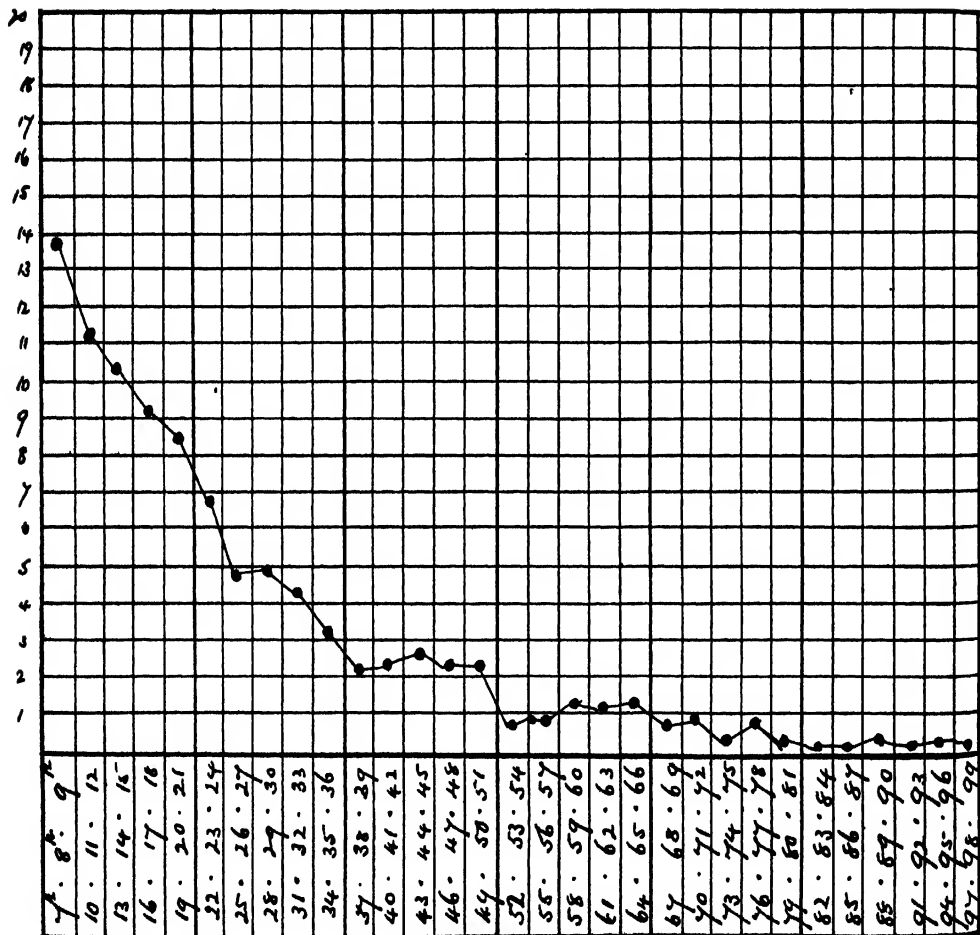


CHART No. 4.

MALARIA ON RUBBER ESTATES. 1912.

Daily Prophylactic Quinine.

Number of Cases, 1,648. Number of Cases recurring, 511 (31.02%). Number of recurrences, 826.



MALARIA ON RUBBER ESTATES. 1913.

Daily Prophylactic Quinine.

Number of Cases, 939.

Number of Cases recurring, 246 (26.2%).

Number of recurrences, 339.

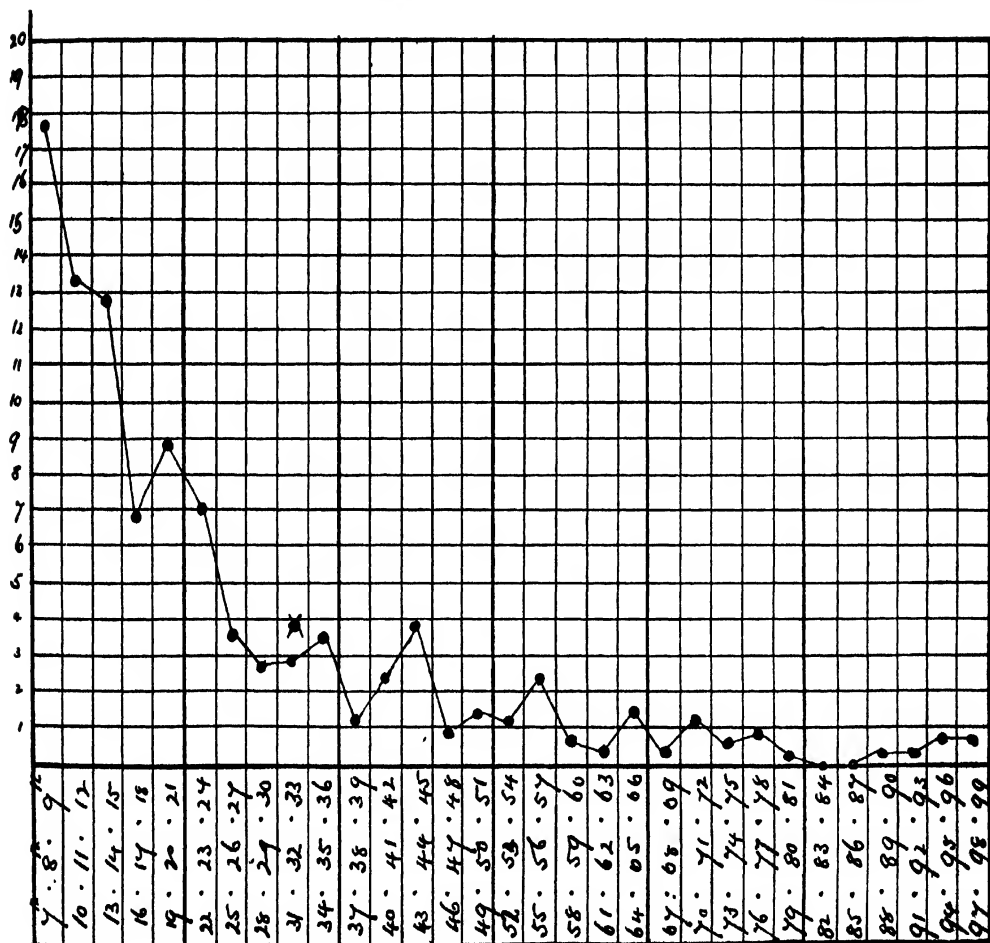
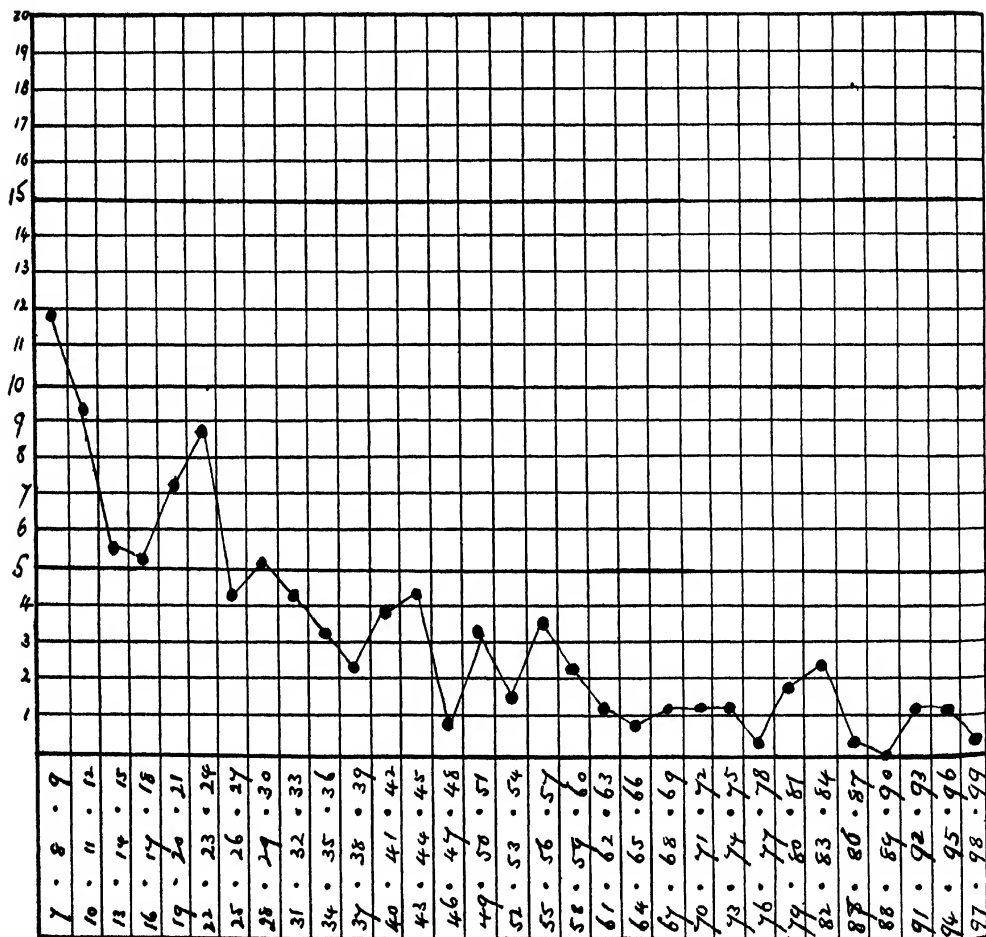


CHART No. 5.

MALARIA ON RUBBER ESTATES. 1914.

Quinine daily—alternate weeks.

Number of Cases, 449. Number of Cases recurring, 153 (34·07%). Number of recurrences, 253.



Sir RONALD ROSS: I am sorry I did not read this paper before coming here this evening. It is a paper that requires study. There are many good ideas in it, and it has raised some important points. The late writer has, I think, done his best, and I am very sorry that he died. I think it would have been very useful if he had been able to answer questions that we could have put to him. I have heard it read out once only, and I did not derive the impression that the writer had made a careful study of the literature of the subject. For instance, in one place he speaks of the non-disappearance of the crescents in the blood in consequence of quinine. Everybody knows they never do disappear so. Well, that is the sort of thing people ought to have read. Then there is another passage in which he talks about the malaria commencing in a place too soon after the first rains, without giving time, so to speak, for the mosquito to go through the larval stage and reach maturity and infect fresh people. That, also, is a subject which has been discussed over and over again. I think that his is not a possible explanation; it would require very careful statistical study to prove it. I think I have attempted to prove elsewhere that a very small rise in mosquitoes above a certain point is likely to cause a very great outbreak of fever. Such a very small rise would elude all observation without the most careful study. How could you expect a busy doctor on an estate to be able to form a conclusion like that, which would require half a dozen careful students to work at properly.

There are many other points that might also be raised. Another point is with regard to the dosage of 5 grains of quinine. I do not believe any people think that 5 grains of quinine in a malarious place are sufficient for prophylaxis. I am quite certain it is not sufficient to prevent relapses in persons in this country. I have just had two midshipmen who have been taking 5 grains of quinine daily, and they have had relapses in spite of it. Then another question—was the quinine good? That is a point which is not mentioned. Quinine is very often faked, and we have our doubts on the question, unless he is quite certain it was up to standard strength. All the same, there are many things I am inclined generally to agree with in this paper. The failure of quinine prophylaxis in places where there is much new infection and re-infection is already known. There is much literature on the subject—for instance, the studies were made in Delhi in India. There the

quinine prophylaxis failed in the presence of repeated recurrent infection. It leads to a point we are often neglecting—that where a patient is infected once he is likely to be infected again afterwards, and more than once afterwards.

This is an important point—the frequent re-infection which the coolies must have suffered from. They are not infected once in the season, but are probably being infected every two or three nights; and you give them quinine in small doses! I take it, quinine is not strictly speaking a prophylactic at all; it is a curative. It does not keep infection out but kills it when it has entered. For prophylaxis one must give quinine in curative doses—5 grains is not a curative dose.

Then, again, another point arises in this paper. I think the author is quite right when he says that quinine given to these underfed coolies will depress their health so that the parasites will multiply more easily. They get very bad dyspepsia, and quinine (he says) makes them sick. That is a rather extraordinary thing, and one does not always meet with such experiences. I remember in India (in my 18 years' service), that we used to give quinine to coolies in much greater doses than 5 grains, before and after meals, and yet it very rarely made them sick. They must have been in a very unhealthy condition, and that would help to assist the parasites, as we know that anything that lowers the health of a patient tends to help the parasites.

Then, again, the question of ankylostomiasis. Apparently all these coolies had that disease. I fancy there was much sickness caused by the ankylostomes which helped the malaria. One can picture to oneself that in these estates the coolies were probably being infected or re-infected every few days by malaria, and their blood was being sucked at the same time by ankylostomiasis, while their digestions were being ruined by quinine! I wonder they lived at all. Quinine is not absorbed at all easily where there is gastro-intestinal trouble.

Still, I am very sorry that the author has died. If he had gone back he would have done very valuable work.

Dr. C. F. HARFORD: The subject of this paper is one that has been debated before in this Society, and I think that the majority of the Fellows of the Society who take an interest in the matter believe that

quinine is a valuable prophylactic against malaria, especially when it is combined with other measures for combating malaria.

Whilst fully recognising the importance of the paper, and greatly regretting the death of the author, attention must be drawn to the inconsistencies which are to be found in it, which cannot fail to detract from the value of the conclusions made by the author.

Take the statement about the prevalence of malaria in connection with rainfall. He seems to point out that there is no relation between the number of mosquitoes present which can convey malaria and the occurrence of malaria itself.

Again, he says in another place that recurrences were extremely common, even on big doses of quinine of 45 grains per day. Here it is not a question whether 5 grains of quinine will keep people from getting malaria, for it is said that 45 grains a day have been given, and yet recurrences take place. It is a question if, under these circumstances, the fever could have been malarial.

One expects after such statements that the author would have abandoned quinine as altogether mischievous, yet further on it is stated, "In either lot when a coolie shewed clinical malaria he had grs. 30 quinine in solution on that day. This had to be done as the coolies would otherwise in all probability have died." So he evidently did not follow to their logical conclusions the observations which he has recorded.

Then we come to what is apparently his practical advice, namely, to take quinine when you think you want it. I regard that as the most mischievous advice which could possibly be given. In cases where quinine administration is associated with blackwater fever it is usually considered to be due to people taking large doses of quinine when they think they want it, and particularly when they have not been accustomed to taking quinine as a prophylactic. All my experience of those living in malarious regions, and especially in West Africa, shews that quinine, if taken regularly in 5-grain doses, is most useful in preventing attacks. I know it will not inevitably prevent malaria, but it has made little short of a revolution in the health of missionaries working in West Africa.

Dr. J. M. ATKINSON: I think it is unfortunate that a discussion of this kind should have occurred at a time of the year when so few

members are able to be present. This is one of the most important subjects that we, as a Society, can discuss. One does not like to criticise the paper, especially as the gentleman who wrote it has died, but as it has been brought up before the Society it is open to us, I presume, to say what we think about it. This paper is the result of three years' experience. Unfortunately, I was somewhat late, and I have not read it all through, but I can talk from an experience of twenty-five years in a malarial district, and I think my experience, which I can prove by figures, will practically controvert this statement that quinine is of no use as a prophylactic. In Hong Kong, which is a highly malarious island, we have tried a series of experiments on the European, Indian and Chinese members of the police force during some years. The results of these experiments have been printed, and can be found in the Blue Books of the Colonial Office. These shewed conclusively that quinine, as a prophylactic, is certainly beneficial in Hong Kong. We tried it on members of the police force after the New Territory was taken over. It was tried for three years, and the result proved that quinine, given in the dose of 5 grains daily, did diminish the incidence of malaria in those who took it. I am not referring to natives only, but to European, Indian and Chinese police, so that we had three nationalities to deal with. Roughly, the results were that 5 grains of quinine given daily, after breakfast, to each member of the force did diminish the incidence of the disease amongst these policemen. We took a certain batch of policemen; and put a certain number on 5 grains, a number on $2\frac{1}{2}$ grains of quinine, and others on arsenic daily, and compared the results. Those having 5 grains shewed a distinct diminution in the number attacked by the disease.

We live in extraordinary times, and this paper is an example of the extraordinary days we live in. I believe that quinine is a prophylactic in malaria, and my personal experience tends to confirm this. In 1887, in Hong Kong, I had an attack of malaria. I had no return of malaria for seven years. I came home on leave in 1894, and had an attack in England—in Lincolnshire—after getting wet through at a cricket match. When I returned to Hong Kong, every summer, from May, when the fever season sets in, up to October, I took 3 grains of quinine every morning, and the result was I have never had malaria since. That is not only my own experience but that of my family too. An old doctor

friend of mine, out in the West Indies for over twenty years, carried out the same procedure with his own family, and practically prevented them getting malaria. I expect that there is some naval surgeon here to-night, and I know it is the custom in the Navy to give quinine grs. 5 every morning whenever they land any men on the West Coast of Africa. I have had this from several of the naval doctors I have met in Hong Kong.

Malaria kills more people in the Empire than any other disease, excepting, perhaps, tuberculosis. This is a subject, more than any other, which should be thoroughly thrashed out by this Society, and I would suggest that the discussion be adjourned until we have a more representative number of members present.

Sir RONALD ROSS: In Hong Kong, what was the spleen-rate among children?

Dr. J. M. ATKINSON: Dr. THOMSON carried out a number of experiments in the spleen-rate amongst the natives in the villages of the New Territory, and, speaking from memory, he found about 33 per cent. of the children had enlarged spleens.

Sir RONALD ROSS: I just point out that that is a comparatively low spleen-rate. The rate in the Federated Malay States is 90 per cent. Five-grain doses of quinine are more likely to be effective in Hong Kong, with a low spleen-rate, than in the F. M. S. with a high one. A high spleen-rate means re-infection going on all the time.

Dr. J. M. ATKINSON: That raises the question of the virulence of malaria in different localities. All diseases vary in their virulence. In epidemics of plague most cases die in the beginning of the outbreak, but as the epidemic abates the attacks become less severe, and I think it may be so with malaria. This paper points to the fact that in the Malay States the disease is much more virulent than in Hong Kong. The virulence of the disease may vary in different localities.

Sir RONALD ROSS: I would write *frequency of infection* rather than *virulence of the parasite*, though both may occur.

Dr. ANDREW BALFOUR: This paper has special interest to me because, thanks to Dr. BAGSHAW, I have the privilege of reviewing all papers on malaria, and I am naturally interested to hear what the Fellows of this Society have to say on the subject.

I looked up one or two of the papers which I have gone through lately in connection with the prophylaxis of malaria, its treatment by neo-salvarsan, and also the methods of administering quinine. I can only ask, like Pontius Pilate of old, "What is truth?" because everybody has contradictory ideas. You find HATORI, in Formosa, lauding prophylactic quinine. You find PARROT, in Algiers, speaking of quinine prophylaxis in schools, and recording excellent results from it. You find an American naval surgeon, called MACGUIRE, finding quinine prophylaxis of little avail. You find Major POLLOCK, a medical officer of the British army in Sierra Leone, carrying out investigations with poor results, and coming to the conclusion that quinine is of very little use. You find STOTT, in Mandalay, carrying out an extensive and careful series of investigations, and coming to the conclusion that it has been over-rated. You find, in Honduras, an American named BARLOW carrying out investigations of a different kind, sterilizing mosquitoes by giving quinine to a fairly large community, with the object of preventing gamete production, and obtaining apparently admirable results. Really, one is perfectly confused between these different views. I am inclined to the view that this is partly due to the fact that many of the investigations are not carried out on strictly scientific lines.

What Sir RONALD ROSS said about making sure of your quinine is only too true. I notice that STOTT, who is a careful worker, tested the solution he gave by means of an hydrometer to see if the strength was correct. That is one point. There are other things in connection with quinine and malaria. You must not only see that your quinine is of proper strength, but be sure that it is taken and that it is fully absorbed. It is a difficult matter to do this under tropical conditions, and I do not know how you can be certain of absorption without an analysis of the urine.

Then there is another point. We all know that if the liver is out of order the quinine is not properly absorbed. I do not think there is any suspicion that these poor Tamils had overloaded livers—rather the reverse; but their absorptive powers may have been much below par.

We want careful, accurate observations made, and, in my opinion, this is work that can only be undertaken by a special commission, provided with every facility for scientific research. The whole question of natural and acquired immunity requires consideration in this connection. I see Dr. LINNELL does just touch upon this aspect of the case in his paper.

As to neo-salvarsan, you find some people lauding this excellent drug as a means of getting rid of relapses. The other day I read a German paper by SUMMER, late P.M.O. at Windhoek, S.-W. Africa, and he declares that neo-salvarsan is of no use for this purpose. After full doses he has had patients suffering from genuine relapses. This is in direct contradistinction to the experience of other writers.

It is quite evident that the whole state of our knowledge on these matters is in a somewhat chaotic condition.

It may be of some interest briefly to record one's own practice and experience. When travelling in malarial regions I always took quinine prophylactically, beginning the dosage before there was any risk of infection, and continuing it for at least a week after quitting the endemic areas. I took five grains a day, replacing one day a week the five-grain by a ten-grain dose, and taking an extra ten-grain dose whenever I knew I had been badly bitten by anophelines, as sometimes happened when my net was rendered useless by weather conditions. I employed the bisulphate or the bihydrochlorate indifferently, cracking the tabloids before swallowing them. The only occasion on which I ever got malaria on these journeys was once on the White Nile, when my servant stole all my quinine and sold it to the crew of the steamer, who evidently firmly believed in the efficacy of quinine.

I remember having to advise an official about quinine prophylaxis, as he was going to a mosquito-ridden post on the White Nile, where there were many chances of infection. He did not want to take quinine every day, so I recommended KOCH's method. He followed it faithfully and never had a day's fever. It must be noted, however, that some years previously, when stationed at Roseires, on the White Nile, he had suffered from a most severe attack of malignant malaria, which nearly killed him. Possibly, therefore, he was immune. I wonder if immunity conferred by a *P. falciparum* infection is effective against *P. vivax* and *P. malariae* infections, and *vice versa*? I do not think this question has

ever been carefully considered ; but the fact is, we want a good test for malarial immunity—a cuti-reaction, or something of that kind. In most cases the immunity conferred is of the slightest so far as we can tell. In many instances it appears to be non-existent.

I hardly like to touch on the question of the method of giving quinine in the presence of Sir RONALD ROSS. I thought for a moment I had found a supporter for his views in the author of this paper, but I do not think Sir RONALD ROSS would claim him as such. If Dr. LINNELL found intravenous injections of quinine of no use, how could he suppose that oral administration would act better ? It might conceivably be true that the latter succeeded when intramuscular injection failed, for the Tamils were debilitated, and their muscles may have lost absorptive power, but it is inconceivable that the oral method proved successful after failure of the intravenous administration.

Dr. LINNELL'S remarks on the use of pineapples are very curious and interesting. I do not think we know much of pineapples. I spoke to Dr. PYMAN about this question, and he said it might be worth while looking into it and finding out if anything can be ascertained by chemical analysis. Pineapples are expensive here, and members of his chemical staff, if uncontrolled, might examine them in an unofficial manner. If these difficulties can be surmounted I may yet be able to report something of value to the Society. At any rate it seems a point worthy of attention.

Dr. F. CHARLESWORTH : I have nothing to say of very great interest on the question of prophylaxis by quinine, and I agree with Dr. BALFOUR the whole question really turns upon investigation into our methods of observation. Until we have scientific investigations on these points, *i.e.*, on the rates of absorption and excretion of quinine, I think we can hardly settle the question whether quinine is of very great value as a prophylactic. I also think, so far as I have seen (I have not read a great deal of the literature on the subject), these experiments, so far as they go, are more convincing when they are negative than when they are positive, unless when combined with a series of observations at the same time upon people who in the same circumstances are not receiving prophylactic treatment.

Dr. F. M. SANDWITH: I think we are bound to criticise this paper—nearly everyone of the speakers has done so. We all regret that the author cannot be here to answer us, but we have to think not of the impression that the paper makes upon the experts in this room, but of what might happen if the paper went out without criticism in our TRANSACTIONS to the 640 Fellows who cannot be here to-night.

Dr. LINNELL seems to have set himself the question, Will quinine alone prevent malaria in Tamil coolies? If he had propounded that question to us before writing his paper, I think everyone in this room would have said it would not be much use trying. I do not know anyone who supposes that a small quantity of quinine, taken every day, with neglect of all other precautions, will protect from malaria. I do not think anyone, even in the nebulous literature to which Dr. BALFOUR has referred, will take that view. The author refers to the preliminary advice which is given to Europeans in this country. Some of us often have to advise men and women going abroad what they have to do to try to prevent malaria. I generally advise them to buy a 2d. tract, which is a chapter written by Sir RONALD ROSS, dealing with some of the minor educative points about mosquitoes and malaria (*A Summary of Facts regarding Malaria*). I always begin by declaring that quinine is not the most important thing. I tell them about the importance of the mosquito net, how it is shaped, and how to use it. I tell them another important thing I am sure we all agree with, that is, that the mosquito does not go to bed with the sun. On the contrary, she wakes up in the interval between the bedtime of the sun and the bedtime of the man; that the mosquito is likely to be frisky and hungry and the man tired, slack, and sleepy. I would rather, if I had a quarter of an hour to advise in, give fourteen and a half minutes on the prevention of the mosquito bites and the last half-minute to quinine, and in that last half-minute I should tell them to take 5 grains of quinine a day, with 10 grains on Sundays, as a help. As regards whisky, they had better start with no whisky at all. If they must drink whisky, then never until the sun goes down. I cannot help feeling myself that quinine alone is quite useless. I know very well that the destruction of mosquitoes on a rubber plantation is very difficult, but we are discussing to-night the domestic and personal prophylaxis of coolies living in huts and what the white man can do.

One of the criticisms I would like to make is, if you use quinine there

is no reason why you should use the sulphate, and many reasons why you should not. Bisulphate is the same price and more soluble—1 in 14 instead of 1 in 800. If you use bisulphate you avoid having to give this acid drink the author speaks of. That will upset the stomach, even if you are fortunate enough to be fortified with "hot curry and rice." He speaks of indigestion and other troubles. Quinine is better after food than before breakfast.

I have seen myself, in the coolie lines in Ceylon, these wretched Tamils come up thinking about the hot sun coming at midday, and shivering at 6 o'clock in the morning. Miserable creatures to look at, nothing but skin and bone, with miserable yellow faces. I was looking at them, not from the question of malaria, but from the point of view of ankylostomiasis. Tamil coolies imported from India into the Malay States are much the same as the people imported into Ceylon, with this difference, that the Tamils prefer the Malay States, so that they are more flourishing there than they are in Ceylon.

I agree with what Dr. HARFORD said, if we are to preach or allow to be preached this doctrine about taking quinine when you want it, you will have in certain parts of the world—West Africa, Central Africa, and East Africa—a crop of blackwater fever. It seems to me that the author's method of giving quinine for malaria is exactly the way I should suppose blackwater fever might be produced. We will not go into the question as to whether blackwater fever is or is not a complication of malaria, but assume that blackwater fever has some association with malaria. I can only say that all the cases of blackwater fever I have ever seen have had the same story of neglect to take regular doses of quinine, and then because the patient thought he wanted it, he takes a large dose and the result is blackwater fever. I do not mean that everybody who does this gets blackwater fever, but every case I have seen has had that history.

It is very interesting to read, on page 249, of a European called "G," who developed blackwater fever after three weeks in the tropics. We all know it is a very rare thing for a European to contract blackwater fever after such a short space of time. I saw a case once after about three months, but I found he had been in other parts of the tropics before, and he had had malaria.

It is interesting to note that blackwater fever was not found among the coolies.

The question of preferring the oral administration of quinine to the intravenous injection Dr. BALFOUR has touched upon. I confess I do not understand it. As Sir RONALD ROSS suggested, perhaps the quinine was not quinine.

The question of neo-salvarsan is very interesting, but those who I know recommend it, recommend that you should follow it by quinine. Why the spleen should be larger in the morning and evening one does not understand. If it was larger in the evening, that might be because the normal temperature is higher. I would like to try careful measurements in the next cases of enlarged spleen that I get.

I hope that when Dr. BALFOUR is investigating pineapples, which may or may not be useful, he will also make investigations about coriander seed, because it would be interesting to know whether it is of any benefit to the human economy.

I do not want to take up the time of the meeting now, but I think although one is not working here in a malarial country, one gets a lot of experience from patients; and when you meet with people who have suffered from perpetual attacks of malaria—and I would add to that blackwater fever too—when you find these people had no knowledge at all about mosquitoes and malaria, and you succeed in educating them, inoculating them mentally, with the idea that the mosquito spells malaria, they go back and live under the same conditions for two or three years, and yet manage never to get malaria and never get blackwater fever. Dr. CHARLESWORTH and I sometimes see people belonging to a missionary society in East Africa who have the history I have shortly sketched. There are many people who have had malaria and a few who have had blackwater fever. These people have learnt the mosquito truth and have gone back and remained two or three years and never had malaria. All these people have taken 5 grains of quinine a day. You may say, if you like, that they are extra careful about mosquitoes, but I cannot help feeling that quinine has something to do with it. I may mention one other case, a young man belonging to another missionary society, from Pemba Island, near Zanzibar. Europeans think so ill of the climate of Pemba that they go to Zanzibar as a health resort. It is prolific in malaria and blackwater

fever. The young man came to me after two years there because he belonged to a society which compelled him to report progress. He said he had had a little indigestion but had not had malaria, no single day of fever. "Were you ever bitten by mosquitoes?" I asked. He said, "Yes, fearfully, hands bitten, etc." I said, "This is not the usual story of Pemba, how do you account for it?" He said, "Well, you told me when I was a recruit that it was possible for a man, if he learnt the things you told him to learn, to live at Pemba for two years without getting fever. I did not believe you, but I thought I would give you a chance. I bought the pamphlet and I read it. I was careful about my mosquito net. I took quinine every day, I never forgot, and I never had one dose of fever." Now that is interesting, but it is only one case of a man living in a place where malaria is common. I said to him, "What about the other white men?" He said, "I have seen two doctors carried out on stretchers since I have been there. They did not seem to believe in mosquitoes, and they did not seem to value quinine." This is only one sample case; one could multiply it. We know a number of persons who have lived a long time in the tropics, and they gain a certain amount of immunity.

I do not think it is quite worth while to accept Dr. ATKINSON's suggestion as it stands. We are at the end of the session, but I will ask the Secretary to take a note of what he has said. This is a subject that might easily be discussed again, and then I hope the war will allow a larger proportion of Fellows to be present, and hear many of the points not thoroughly discussed to-night. In the meantime I do not want this paper to go out to our Fellows with the idea that we accept the doctrine laid down by the author.

NOTES AND COMMENTS.

TREASURY DEPARTMENT, U.S. PUBLIC HEALTH SERVICE,
BALTIMORE, MD., U.S.A.

May 24th, 1915.

The EDITOR of the TRANSACTIONS of the Society of Tropical Medicine
and Hygiene,

11, Chandos Street, Cavendish Square, London, W., England.

DEAR SIR,

I enclose herewith a note, and query as well, on the question of the nature of the immunity given by one attack of yellow fever, which I should be glad to have appear in the TRANSACTIONS, in the hope that I may receive an answer to my query.

I think the note should be of interest to any of your members interested in yellow fever.

Very truly yours,

HENRY R. CARTER,

Assistant Surgeon-General U.S. Public Health Service.

IMMUNITY IN YELLOW FEVER.

That yellow fever produced only a temporary immunity and recurrent attacks are common has been generally held, by the laity at least, in places in which it was endemic. This also is asserted, without discussion, by the Pasteur Institute working at Rio, who state categorically that the infection of endemic centres is kept up by recurrent attacks among the natives. This statement is accepted by SEIDELIN, BOYCE, and some other recent writers.

On the contrary, writers studying this disease outside the area of its endemicity hold that the immunity conferred by one attack is, with rare exceptions, permanent, and have based sanitary measures on this doctrine.

I know of no observations in confirmation of the first doctrine (except

some by SEIDELIN based on the causal relation of his *Paraplasma flavigenum* to yellow fever), and would be glad to know if there be any. I am of opinion that the negative testimony of observers working in yellow fever outside the area of its endemicity, *i.e.*, that they have not observed attacks of yellow fever in those who have had it previously, would not be accepted unquestioned by those who hold the doctrine of temporary immunity. It would be discounted by them on account of these observers, because of their preconceived opinions, being little apt to recognise light cases of yellow fever occurring as secondary cases, and this although in the aggregate the number of such negative observations is large. I present, however, the following epidemiological study, which is not open to this objection, and which, I think, throws some light on the subject.

If recurrent attacks are common and are infective to *Stegomyia fasciata*, the presence of any considerable number of people suffering from such attacks in a community susceptible to yellow fever during hot weather, and with active stegomyia mosquitoes abundant, should lead to an outbreak of yellow fever. This could not escape recognition. The same is true of "carriers," the existence of which is also predicated as common.

Now, from 1889 to 1897 inclusive, the Plant S.S. Line brought passengers from Havana to Florida—Key West and Tampa. Key West is six or seven hours and Tampa twenty-four hours from Havana. There was no bar to any passenger "immune to yellow fever by previous attack or ten years' residence in an endemic focus." Many such passengers came: Cubans under their ten years' residence, Americans under certificate of previous attack. In addition, two officers were compelled to go ashore at each trip to enter and clear the ship, and members of the crew were shipped in Havana at every trip. I can only estimate the number, although I was very familiar with the operation of this line, but would put it at from twenty-five to fifty per week. Taking only the quarantine season, April 15th to Nov. 1st—twenty-eight weeks—that lesser number gives 700 per annum, or 6,300 for the nine years.

Note that this very considerable number of people—and I have taken minimal numbers—came in hot weather to towns in which stegomyia were abundant and active, and where people susceptible to yellow fever were also abundant. If then any considerable proportion of them were

infective to stegomyia, there should have been outbreaks of yellow fever in Florida during these nine years. There was none. We must conclude then that no considerable number of people infective to stegomyia were among them.

The only question is then, to what degree were men susceptible to yellow fever liable to contract yellow fever in Havana during this period? We have a check from the vessels from that port whose crews had *not* had yellow fever coming to our quarantine stations. They frequently brought cases of yellow fever, or yellow fever developed on them after arrival. I have not the numbers at hand for all stations, but at the Dry Tortugas quarantine in 1895 the combined crew-lists of the vessels from Havana were about 450. Fully one half of these men were aboard steamships which lay across the bay from Havana and allowed no shore liberty to their crews. Only one of them shewed a case of yellow fever—an officer who had to go ashore on ship's business. Among the remainder—about 225—twelve cases of yellow fever developed. The experience at the other U.S. quarantine stations on the Gulf of Mexico, up to 1898, with Havana vessels, was similar to that at Tortugas. Unquestionably, then, men susceptible to yellow fever could, and did, contract it in Havana during this period, and if any considerable proportion of these people who came by the Plant Line into Florida had been susceptible to yellow fever many of them would have contracted it. From what has just been said, no considerable number of them did develop it in Florida, and hence did not contract it shortly before leaving Havana.

Compare these observations:—

Two hundred and twenty-five (about) people, who had not had yellow fever, from Havana, gave twelve cases, everyone of which would have been infective to stegomyia.

Six thousand three hundred people from the same place, during a period covering the same time, gave no evidence of infecting stegomyia mosquitoes.

This is negative evidence—the nature of the case admits of no other—and negative evidence is convincing in proportion to its mass. Whether it is of sufficient mass to be convincing must be left to the reader. I believe (which is not evidence) that had the Spanish-American War been postponed its mass would have been greater.

There are some other epidemiological observations consistent with the doctrine of permanent immunity, but none give stronger evidence than the above.

INTRAVENOUS INJECTION OF QUININE.

The EDITOR of the TRANSACTIONS of the Society of Tropical Medicine
and Hygiene.
SIR,

With reference to a paper by Dr. THOS. E. WRIGHT, entitled "Thirty Cases of Malaria Estivo-Autumnal treated with Quinine, Intravenously," reviewed in Vol. 5, No. 6, 1915, *Tropical Diseases Bulletin*, I would like to mention a method tried by me on four cases with satisfactory results. Dr. WRIGHT recommends the intravenous injection of quinine hydrochloride in a dilution of 250 to 300 c.c. of saline solution. This may possibly be a safer method, but I have seen no harm result from the intravenous injection of the contents of the ordinary ampoules (B. & W.) containing 10·34 grs. of quinine hydrochloride in 1 c.c. without any dilution whatever. The injections were performed slowly. All that was noticed was a slight increase of the force and frequency of the pulse, which only lasted a few minutes; a very slight increase of frequency in the rate of respiration; no cough or other disturbance.

In one of the four cases a second injection was given within three hours of the first. The effect on the course of the disease was marked, and the patients made uneventful recoveries on quinine continued by the mouth.

Of course, I have only tried this method in these few cases, but so far see no indication why I should not continue to do so when occasion arises. It is a simple and rapid method, and with the exception of putting on a pad of cotton-wool and a few spiral bandages, takes no more time than an ordinary hypodermic injection.

The administration of quinine in this manner, when intravenous injection is desired, should be particularly useful for troops in the field.

I am, Sir, yours faithfully,

J. O. SHIRCORE, M.B., M.R.C.P. (Edin.),

Medical Officer East Africa Medical Service.

Mombasa, 15th June, 1915.

LIBRARY NOTES.

Dr. LLEWELLYN POWELL PHILLIPS, Professor of Medicine in the Egyptian Government School of Medicine, Cairo, has rendered a distinct service in bringing out a new book on Amœbiasis and the Dysenteries.*

Dysentery is one of the most important of tropical diseases, and many different varieties of it are now recognised. A book dealing with all these must therefore be useful. The classification adopted by Dr. PHILLIPS is as follows :—(A) Protozoal dysenteries and those caused by other animal parasites : (1) Amœbic dysentery (Amœbiasis); (2) Ciliate dysentery (Balantidiasis); (3) Flagellate dysentery (Lamblia, Tetramitus, etc.); (4) Bilharzial dysentery. (B) Bacillary dysentery. The author might with advantage have incorporated the dysenteric symptoms connected with kala-azar and malaria in his general table, instead of only mentioning that these diseases sometimes give rise to such symptoms. The spirochætal form, of course, only requires a mere mention, as the association of this parasite with dysentery has by no means been distinctly proved.

In Chapter 1 the historical details of the discovery of amœbæ in dysentery, and the gradual recognition of the part this parasite plays in producing the symptoms of the disease is well dealt with. Chapter 2 deals with the description and life history of the parasitic amœbæ; Chapter 3 with the lesions of amœbiasis as affecting the intestine, liver, brain, etc. Chapter 4 with the clinical description of intestinal amœbiasis; Chapter 5 with amœbiasis of organs other than the intestine—acute hepatitis, liver, abscess, etc.; and Chapter 6 with the treatment of the disease.

Ciliate dysentery (Balantidiasis) is dealt with in Chapter 7; Flagellate dysentery in Chapter 8; Bilharzial dysentery in Chapter 9; while the last three chapters of the work are devoted to Bacillary dysentery.

There is also a bibliography and an index, the book, with these, running to 147 pages. It will thus be seen that the book is a small one, and the difficulty in such a case is what to insert and what to leave out.

**Amœbiasis and the Dysenteries*, by LLEWELLYN POWELL PHILLIPS, M.A.. M.D., F.R.C.P. & S., Professor of Medicine in the Egyptian Government School of Medicine, Cairo. London: H. K. Lewis, 136, Gower Street, W.C. 1915. 6s. 6d. net.

Dr. PHILLIPS has met this difficulty well, a study of the work shewing a very careful and accurate synopsis of all the important points. In addition to this, the author has also been able to use his own personal experience of the disease, and this adds, of course, to the value of the manual. Perhaps one of the most interesting chapters is that on flagellate dysentery, a subject upon which more work is certainly required. Many believe that the different flagellates found in the intestines are non-pathogenic, though some cases would seem to shew that, in certain instances at least, this is not so.

The part on Bacillary dysentery is also very well written, and the definite pathology and lesions of this type of the disease are very clearly dealt with.

The absence of illustrations, due to the pressure caused by the War, is to be regretted. Good diagrams of the various flagellates, for example, would have been of great value. However, the author may be able to remedy this defect in a future edition.

The work is a very good one, is excellently written, and can be thoroughly recommended.

G. C. LOW.

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